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APRIL, 1934

PUBLISHED MONTHLY BY THE AMERICAN MEDICAL ASSOCIATION
DEARBORN STREET, CHICAGO, ILLINOIS

Entered as Second-Class Matter ... 1917, at the Post... Act of Congress of March 3, 1879. Authorized for mailing at special rate of postage provided for in Section 1103, ... of October 3, 1917, authorized ...

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Archives of Dermatology and Syphilology

VOLUME 29 APRIL, 1934 NUMBER 4

INTRADERMAL TESTS IN RELATION TO ARSPHENAMINE DERMATITIS

A STUDY BASED ON TWO HUNDRED AND FIFTY-SIX CLINICAL CASES

A. BENSON CANNON, M.D.
AND
MARIE B. KARELITZ, M.D.
NEW YORK

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From the Vanderbilt Clinic, Columbia University College of Physicians and Surgeons.

Read at the Fifty-Sixth Annual Meeting of the American Dermatological Association, Chicago, June 9, 1933.

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INTRODUCTION

In pursuance of studies begun several years ago with the idea of investigating the rôle of arsenic in the pathogenesis of certain cutaneous lesions of doubtful origin, we decided to investigate the reactions in a series of patients under treatment with the arsphenamines, selecting, as far as possible, patients who had shown some form of intolerance to preparations of this group. For purposes of comparison we also studied some patients who had tolerated the drug without ill effects and others who had received arsenic in other forms.

In earlier studies we had centered our attention on cutaneous manifestations as toxic phenomena, investigating particularly the retention and excretion of arsenic in relation to dermatitides and disturbances of pigmentation. In the present study we attacked the problem from a different angle, desiring to see whether allergic factors played any considerable rôle in the diverse responses of different patients to one and the same drug. For this purpose we carried out intradermal tests on 256 patients, all of whom were in attendance at the department of dermatology of the Vanderbilt Clinic between the years 1928 and 1933 inclusive. Thirteen of these we excluded from consideration in analyzing our results because the patients absented themselves from the clinic for considerable periods immediately after the tests, and we wished to record only first-hand observations.

Of the 243 valid cases remaining, 209 represented various stages of syphilis. The majority were cases of early syphilis, but there were also instances of tertiary, latent, visceral and cardiovascular syphilis, neurosyphilis and congenital syphilis. The remainder were cases of other diseases, including eczema, psoriasis, keratosis palmaris et plantaris, vitiligo, lichen planus, scleroderma, furunculosis, pemphigus and premycosis fungoides. Of the 209 syphilitic patients 195, or all but 14, had received treatment or were under treatment with the arsphenamines at the time of the first intradermal test. Fourteen either had received arsenical preparations in other forms or were patients with early syphilis as yet untreated. Of the nonsyphilitic patients the majority had either a history of arsenical medication or evidences of arsenic in the blood or urine. Among the latter group were some industrial cases. In a few instances no evidence of arsenic had been disclosed in the history or in the laboratory tests.

Of the 195 syphilitic patients who had received some treatment with arsphenamine before their first intradermal test, 68 had tolerated the arsphenamine without complication prior to the first test, and 127 had manifested some sign of intolerance. Of the latter, 95 had had severe manifestations in the form of nitritoid crises, dermatitis, jaundice, neuritis or keratosis palmaris et plantaris. In some of these instances milder reactions had preceded the more severe ones. Thirty-two patients had had only mild reactions prior to the first intradermal test, such as nausea, vomiting, headache, general malaise, transitory outbreaks of urticaria and fever of short duration. In a few instances, symptoms originally suspected of being due to arsphenamine medication were so complicated by other factors that it was impossible to determine the rôle—if any—played by the arsphenamine.

METHOD AND TECHNIC

Intradermal tests with the arsphenamines were performed on all the 256 patients. Patch tests were also done on a considerable number. Old arsphenamine, neoarsphenamine and silver arsphenamine were used as a routine, and sometimes tryparsamide was employed in addition. The lower dilutions were standard solutions identical with those prepared for intravenous medication (old arsphenamine, alkalinized and diluted 1:200 in distilled water; silver arsphenamine, 1:200, and neoarsphenamine, 1:100, in distilled water). The higher dilutions, ranging from 1:250 to 1:200,000, were prepared by adding distilled water to the standard solutions. One-tenth cubic centimeter was injected with a tuberculin syringe and a 26 gage needle, usually into the skin of the external aspect of the upper arm. Sometimes the forearm was used, and occasionally the thigh. For controls we used distilled water and solution of potassium arsenite; alkalinized old arsphenamine was further controlled by the injection of a solution of nonalkalinized old arsphenamine.

Time and Number of Tests.—In all, 411 intradermal tests,[1] or 1,586 separate test injections, were made, exclusive of the controls. The tests were done at different intervals in relation to the clinical condition under investigation. Some were done during an arsphenamine dermatitis; others, at various periods after the eruption had cleared up. In cases in which intolerance to arsenic had manifested itself in forms other than cutaneous eruptions, as, for example, in neuritis, jaundice or immediate symptoms of shock following an injection, or in cases of repeated minor disturbances, tests were likewise attempted at various intervals from

1. The word "test," unless otherwise specified, will be used in this article to signify a group of several test injections of the different arsphenamines performed on a single patient on the same day.

the onset or termination of the symptoms, and in the majority of cases were repeated on the same patient, in many instances 2 and 3 times. In a considerable number, from 4 to 7 successive tests were made on the same patient. The greater part of the syphilitic patients were under treatment with the arsphenamine at the time of the tests, but others had had no treatment for several months or even years prior to the first test, and still others were patients in the early stages of the disease who had come for a diagnosis but had not yet received their first treatment. It was hoped that the testing of a considerable series of patients under the variety of conditions described and the repeating of tests whenever possible might help to offset the element of chance in the outcome and interpretation of the tests.

Observation After Tests.—The tests were all performed and the patients followed personally by us at the Vanderbilt Clinic over the period between 1928 and the spring of 1933. Each patient was kept under observation from one to two hours immediately following the test injections, and any immediate reactions were recorded at this time. We endeavored to have every patient return to the clinic for observation within from twenty-four to forty-eight hours after the test, and all were given explicit instructions for recording any manifestations appearing on the test sites between the time of injection and the next visit to the clinic. Any subsequent manifestations or any changes in the earlier manifestations were followed and recorded by us at frequent intervals. The overwhelming majority of the patients were followed for at least several months, being under treatment for syphilis or some other condition, and some were under observation for one, two and three years. Patients who received intravenous injections of arsphenamine after having had an intradermal test were watched with especial care to see whether there was any evidence of their having been sensitized by the intradermal injection.

TYPES OF REACTIONS

Immediate, Early and Delayed Reactions.—Immediate (traumatic) reactions appeared at practically all the sites of injection in the form of a small wheal, a blotch of erythema or a wheal surrounded by a halo of erythema. These reactions were transient, usually disappearing within an hour or two, though occasionally they lasted into the next day. They appeared with equal uniformity at the sites where arsphenamine had been injected and at the control sites. Of the minor differences observed among the individual drugs, we found neoarsphenamine to be slightly less irritating on the whole, while solution of potassium arsenite often produced a larger area of erythema than any of the arsphenamines. Tryparsamide usually produced only a wheal, occasionally with erythema.

One or more "positive" reactions of various grades of intensity but distinct from the immediate reactions and appearing from twenty-four hours to several weeks after these had subsided, occurred in 84, or slightly less than one third of the persons tested. The most characteristic of the positive reactions, when fully developed, was a bluish-red papule or nodule, varying from the size of a pea to that of a bean, surrounded by a halo of erythema, the whole comprising an area of from 1.5 to 4 cm.

In their original form the nodules often appeared suddenly, being noticed first by the patient as "like mosquito bites;" then they increased in size and became indurated; the earlier pink color took on a reddish or violaceous tinge, and a red halo appeared and spread, sometimes accompanied by diffuse edema and more or less induration. These reactions usually attained their maximum within from two to four days after their first appearance and remained for varying lengths of time, a considerable number persisting for several months. The majority, however, subsided gradually within from two to six weeks, leaving a scaling pigmented spot which sometimes did not fade until weeks or months afterward.

On these typical reactions there was sometimes superimposed a scaling or lichenification (occasionally vesiculation) over the entire area. In a few instances instead of a definitely circumscribed papule or nodule there appeared a diffuse area of erythema and edema, growing more indurated toward the center, the whole surface being covered with a typical eczematous dermatitis, with vesiculation and oozing. These reactions were invariably more extensive than the others, those from several adjacent test sites coalescing to form inflammatory areas from 10 to 12 cm. or more in diameter.

"Positive" Reactions.—In studying these various reactions we found that it was difficult, if not impossible, to determine the relative significance to be accorded manifestations showing so many gradations of intensity as well as differences in type. It seemed necessary, however, to make some more or less arbitrary classification for our temporary convenience, the more so as we found little uniformity among previous investigators whose reports on this subject had come to our attention.

We therefore considered as definitely or strongly positive all reactions of the types heretofore described which persisted for one week or longer, and as weakly positive or doubtful any reactions which involuted completely in less than one week. We also considered as doubtful certain very mild manifestations, such as infiltrations of 0.5 cm. or less at the site of the injection, noticeable only on palpation, even though a few of these persisted for from seven to eight days. A number of patients showed reactions which appeared to be strongly positive, but

which we were unable to keep under observation for more than a few days because the patients either failed to return to the clinic or else returned after a considerable lapse of time. These reactions were also termed doubtful, although the presumption was strong that they remained for seven days or longer. Erythema or pigmented spots left over from the immediate traumatic reactions were disregarded. In estimating the duration of the positive reactions we counted only the duration of the papule, nodule or induration or of the area of dermatitis, disregarding residues of pigmentation or slight scaling. "Positive" hereafter, unless otherwise specified, will be used to include both strongly and weakly positive reactions. No reaction has been termed "negative" unless observed for at least one week following the injection.

Of the 411 intradermal tests performed, 123 produced positive reactions at one or more of the sites of injection. Altogether 310 separate sites of injection gave positive reactions. In 94 (76.4 per cent) of the tests producing positive reactions, the reactions manifested themselves within seven days from the time of injection, the majority of them appearing between the second and the fifth day. In the remainder (29, or 23.6 per cent) the reactions appeared later than seven days after the injection: 17 during the second week, 8 during the third week, 3 during the fourth week and 1 after nearly seven weeks. There seemed to be no uniform relation between the time of appearance of the reactions and their duration. Sometimes the earlier ones remained in evidence longer than the delayed ones. Sometimes the reverse was true. The reactions of an individual patient to the different drugs appeared nearly always simultaneously on the sites of injection at the same time; when differences were noted, they were so slight as to be negligible.

Reactions to First and Later Tests Compared.—In the cases in which 2 or more tests were done at different times on the same patient, the majority (roughly two thirds) showed either consistently positive or consistently negative reactions on repeated testing; but 27 patients, or about one third of the group, after reacting negatively to the first test, subsequently gave positive reactions when the tests were repeated. In only a small number of cases (10) did there appear to be any acceleration of the reaction time when the test was repeated. In a still larger number either subsequent reactions were more tardy than the first, or else (in some cases in which from 4 to 7 tests were performed) there was no uniformity, the time of appearance running for example as follows:

	The Reaction Appeared in						
Case	First Test in	Second Test in	Third Test in	Fourth Test in	Fifth Test in	Sixth Test in	Seventh Test in
223.....	1 day	8 days	2 to 3 days	1 day	0	0	0
215.....	Negative	3 days	7 days	7 days	5 days	7 days	8 hours
191.....	2 days	1 day	8 days	11 days	0	0	0
121.....	Negative	Negative	1 day	7 days	7 days	1 day	0

These differences, together with variations in the response to the different drugs, will be taken up in greater detail in connection with the clinical comment.

TESTS IN PATIENTS WITH AND WITHOUT ARSPHENAMINE THERAPY

Intradermal Tests in Tolerant as Compared with Intolerant Patients.—As we now examine the outcome of the intradermal tests in relation to the patients' tolerance or intolerance of arsenic medication, we find that of the 95 syphilitic patients who had received arsphenamine treatment and who had manifested severe symptoms of intolerance prior to the first intradermal test, only 24, or less than one fourth, gave positive reactions to the first test, while 71 showed completely negative reactions. Of the 32 patients who had shown only milder symptoms of intolerance prior to the first test, 26 gave negative reactions, and 6 gave positive reactions to the first test, only 1 of the latter being strongly positive. Altogether, taking the 127 patients whose symptoms of intolerance, either major or minor, could be definitely attributed to arsphenamine, and ignoring the cases in which other causes might be incriminated, only 30, or 23.6 per cent, gave any sign of hypersensitiveness to the first intradermal introduction of the drug, while 97, or 76.4 per cent, showed entirely negative reactions. Of the 68 patients who had tolerated arsphenamine medication without any history of complications of any kind, all but 5 gave negative reactions to the first intradermal test and only 2 of the 5 gave strongly positive reactions. Two others, although showing negative reactions to the first test, later gave positive reactions when the tests were repeated. Thus when we compare the results in the two groups of tolerant and intolerant patients, it appears that the intolerant group gives a relatively higher percentage of positive cutaneous tests than the tolerant group, but that the absolute percentage is too small to permit conclusions on this basis alone.

It will be remembered that in the overwhelming majority of the patients the reaction remained either positive or negative, as the case might be, when the tests were repeated. Let us turn for a moment, however, to the smaller group of intolerant patients (19 in all) who, though they showed negative reactions to the first test, gave positive reactions when the tests were repeated. There was a possibility that this difference might be accounted for by the time at which the test was performed in relation to the clinical symptoms of intolerance. Certain investigators (Kagelmann, Sézary and Mauric, Puente and Cordiviola, also Garnier, in some instances) found that their patients with arsphenamine dermatitis did not give positive reactions, for the most part, until some time after the dermatitis had healed, although Garnier also found some instances in which tests done during the dermatitis resulted in

strongly positive reactions. We found that two thirds of our negative first tests on this group had been done during active manifestations of intolerance, while one third were performed after the symptoms had cleared. When these patients later gave positive reactions on repeated testing, it transpired that all the positive reactions, without exception, occurred after the patients had recovered from their clinical symptoms of intolerance. Positive reactions were not obtained uniformly, however, from patients with dermatitis after the dermatitis had cleared, as some of these patients, in addition to 1 or more positive reactions, also gave negative reactions to some of the later tests.

In order to view the same problem from a slightly different angle we separated the results of our tests in all our 76 patients who had had an arsphenamine dermatitis, to see whether a larger proportion of positive reactions was obtained during the dermatitis or while the skin was clear. Included in these figures are 13 tests on 7 patients in whom a dermatitis first developed after they had had 1 or more intradermal tests. Sixty-five tests in all were done at various stages of the dermatitis, and 85 in the absence of cutaneous manifestations. Of the tests performed during the dermatitis, 48, or three fourths of the total, were negative, while of the ones performed when the skin was free from eruptive manifestations, 38 were negative and 47 positive. One is tempted to recall here the explanation suggested by Milian: that when the dermatitis is just clearing up but still present and visible, one seeks an area where the test will be easily visible, namely, an area which has remained exempt from dermatitis and in which the vasomotor mechanism is, therefore, intact. Later on, after the dermatitis has disappeared, one chooses a site indifferently, and thus it not infrequently happens that this coincides with an area of previous dermatitis; this area, though objectively sound, has latent nerve lesions which become patent at the slightest vasodilator stimulation.

We have discussed dermatitis first in relation to the tests, since it constituted the most frequent single complication from arsphenamine medication. An analysis of the responses of patients with other severe symptoms of intolerance, principally jaundice and neuritis, did not disclose any greater uniformity in positive or negative reactions than did the group with dermatitis. This was true both as to the proportion of positive results to negative ones and as to the outcome of the tests in relation to the presence or absence of clinical symptoms. To save space we have omitted details of these various counts.

Tests in Patients Without Arsphenamine Therapy.—Besides the relatively large group of syphilitic patients treated with one or more of the arsphenamine preparations there were 48 patients who had received no arsphenamine prior to the first test. These were for the most part

patients with various diseases of the skin accompanied either by a history of treatment with an arsenic compound, such as solution of potassium arsenite, or by laboratory findings of arsenic in the blood, urine or skin. Two patients were painters who had worked with paris green or other preparations containing arsenic, and a third was a furrier. These 3 had exceptionally high amounts of arsenic in specimens of urine submitted for analysis, while in 18 others the blood or urine also showed varying amounts of arsenic the source of which could not be traced. Seven patients gave no evidence of arsenic, either in the history or in laboratory tests.

Of these patients, most of whom had cutaneous eruptions or signs of retention of arsenic in the system, but who gave no history of having received arsphenamine medication, 22, or 45.8 per cent, gave positive reactions to 1 or more of the intradermal tests, and 26 gave only negative reactions. When we compared these figures with the results obtained in the group of patients previously treated with the arsphenamine preparations, we found altogether 202 patients treated with arsphenamine, several of whom did not have syphilitis but had received arsphenamine for other conditions. Of this number, 62, or 30.7 per cent, gave positive reactions to 1 or more tests. Thus it will be seen that a considerably higher proportion of positive reactions appeared in the patients without previous arsphenamine medication. This suggests the possibility of a desensitizing effect from the intravenous introduction of the drug, which has been noticed by other investigators as well. This point together with the question of specificity of the reactions to arsphenamine and other arsenical preparations will be taken up in subsequent sections.

We have preferred to report first the more general aspects of our problem, including the distribution of positive and negative reactions among the various major groups of patients studied. For this purpose we have considered primarily the test as a unit, regardless of the number of separate injections or the variations in response to the individual arsphenamines. In the next section we shall take up in more detail the question of specificity, together with the comparative results obtained with different dilutions of the drugs and with the patch method as compared with the intradermal method. We shall also discuss the possibilities of sensitization and desensitization as applied to the problem of continued treatment for syphilis.

THE INTRADERMAL TEST AS AN AID IN DIAGNOSIS AND PROGNOSIS OF COMPLICATIONS FROM ARSPHENAMINE THERAPY

The Test in Diagnosis: Specificity.—To be of practical value, a cutaneous test must first of all be safe for the patient, and it must justify itself either as a diagnostic or as a prognostic aid. In certain so-called allergic dermatoses, tests—especially patch and scratch tests—have

proved themselves of value in determining which of several possible substances is the offending one. When we approach the problem of diagnosing disturbances which have already appeared during arsphenamine therapy, we see that in the group of cases under investigation, positive reactions occurred in a considerable number—30 out of a total of 127, or 23.6 per cent—decidedly more than in the group of patients who had shown no ill effects from similar treatment. When we consider only the patients with dermatitis, we find that of the 76 patients whose dermatitis could be definitely attributed to an arsphenamine, 37, or 48.7 per cent, gave positive reactions to 1 or more intradermal tests. Although even this percentage is smaller than desirable, the reaction might still be of some value if it proved itself specific; it might help to determine not only when the eruption was due to arsphenamine and not to some other cause, but also whether one particular arsphenamine was responsible, while another one might be administered with impunity.

Reactions to Different Arsphenamines: We shall examine in greater detail the positive reactions obtained in this group of patients, namely, the 37 who had had an arsphenamine dermatitis and who had given positive reactions to 1 or more of the intradermal tests, before, during or after the dermatitis. We found only 5 who reacted positively to the intradermal injection of the same arsphenamine which had produced the dermatitis and negatively to the injection of other arsphenamines. On the other hand, there were 3 patients who gave no reaction to test injections of the arsphenamine which led to the dermatitis, but positive reactions to tests with other arsphenamines. Of these 3 patients, 2 did not receive any other arsphenamine, and the remaining 1 subsequently tolerated a second arsphenamine without mishap. As to the other patients of the group, some gave positive reactions uniformly to all the arsphenamines injected intradermally whether they had been treated with these or not, while others who had tried several different arsphenamine preparations and in whom cutaneous rashes had developed after each, gave positive reactions to one of the preparations but not to the others.

The lack of accord between a patient's reaction to arsphenamine therapy and his response to an intradermal injection of the same arsphenamine may be seen again when we compare the number of positive reactions to each drug with the number of patients treated intravenously with that drug. Thus, 110 patients were treated with neoarsphenamine, but only 92 positive reactions to intradermal injections of neoarsphenamine were observed, while there was a total of 103 positive reactions to old arsphenamine although only 47 patients were treated with this drug. For silver arsphenamine the total number of positive

reactions was still higher (111); 75 patients had received silver arsphenamine intravenously. As explained in the beginning, tests were performed in equal numbers with all three arsphenamines.

From table 1 one may also compare the number and percentage of cases of dermatitis for which the various arsphenamines were responsible—the figures for neoarsphenamine leading and those for old and silver arsphenamine assuming about equal proportions. Thus the drug responsible for the highest percentage of cases of dermatitis (neoarsphenamine) produced the lowest percentage of positive reactions to intradermal injections, while the drug yielding the lowest percentage of cases of dermatitis (silver arsphenamine) caused more positive reactions than either of the others. As we have stated previously, the positive reactions to a certain arsphenamine occurred by no means uniformly in the

TABLE 1.—*Number of Cases of Dermatitis from the Different Arsphenamine Preparations Compared with the Number of Positive Reactions to Intradermal Injections of the Same Drugs**

	Neo-arsphen-amine	Old Arsphen-amine	Silver Arsphen-amine
Number of patients treated with each drug	110	47	75
Number of cases of dermatitis from each drug	41 (37.3%)	11 (23.4%)	17 (22.7%)
Number of positive reactions to intradermal injection of each drug	92	103	111

* The figures given in this table of necessity involve some duplication, since a number of patients had received different arsphenamines at different times, and the several cases of recurrent dermatitis are included. On the other hand, 12 additional cases of arsphenamine dermatitis are not listed here because the patients had received some or all of the arsphenamine responsible for the dermatitis before their admission to the clinic, and it could not be ascertained with certainty which preparation had been used.

patients treated with that preparation, nor even in those whose dermatitis could be traced directly to it. Twelve additional cases of arsenic dermatitis in patients with syphilis treated intravenously are not listed here because the patients had received some or all of the medication responsible for the dermatitis before their admission to the clinic, and it was often impossible to get complete histories from outside sources. If all the facts in these cases were known, it is not unlikely that the figures for neoarsphenamine would rise still higher, since that is the drug most commonly used by the general practitioner in the treatment of early syphilis.

It should also be noted that of these 306 positive reactions following intradermal injections of the arsphenamines, all but 36 were obtained with dilutions of less than 1:1,000, and mostly with dilutions of 1:100 and 1:200. There were 16 positive reactions from dilutions ranging between 1:1,000 and 1:2,000, 11 positive reactions from dilutions between 1:5,000 and 1:7,500, 7 positive reactions in the group from

1 : 10,000 to 1 : 20,000, and only 2 positive reactions from dilutions of 1 : 100,000 and 1 : 200,000 respectively. Neoarsphenamine did not give any positive reactions when injected in dilutions above 1 : 7,500, while old arsphenamine gave 6 positive reactions, and silver arsphenamine 3, in the higher dilutions. All the reactions from the higher dilutions occurred in 7 patients—5 with arsphenamine dermatitis, 1 with keratosis palmaris et plantaris and 1 with scleroderma, the latter 2 without a history of arsenic medication.

Differences in Reaction to Arsphenamines and to Other Arsenic Preparations: Although solution of potassium arsenite was used regularly as a control in the tests, we met with only 1 instance in which it produced a positive reaction. This was the case of a woman admitted with scleroderma of one year's duration. There was no evidence of syphilis, and no history of any arsenic intake, although minute quantities of arsenic were found in specimens of the blood and urine. A first intradermal test resulted in positive reactions to solution of potassium arsenite and to all the arsphenamines in standard dilutions. A second test nine months later showed positive reactions to all the arsphenamines, as before, but the reaction at the site where solution of potassium arsenite had been injected remained negative. One might have expected positive reactions in patients who stated that they had taken solution of potassium arsenite and who were admitted with cutaneous eruptions apparently due to the medication—especially those with high amounts of arsenic in the blood and in the urine—but this theory did not materialize.

Positive reactions to tryparsamide were shown by only 2 patients, neither of whom had ever been treated with this drug. One of the 2 had had arsphenamine dermatitis; the other had had no arsenic therapy and no cutaneous eruption. Both patients gave strongly positive reactions to all three arsphenamines.

Nonalkalinized old arsphenamine gave the same results as did the standard alkalinized solution, with a single exception: One patient with a chronic eczema gave a weak reaction to the alkalinized solution but a negative reaction to the nonalkalinized solution. A patch test with the alkalinized solution was also negative.

If the cutaneous reaction is at all specific, it does not seem to be a question of trivalent as compared with pentavalent compounds, for the pentavalent tryparsamide and the trivalent solution of potassium arsenite produced uniformly negative reactions, regardless of whether or not the patient had received previous arsenic medication. It is true that with the 3 exceptions already mentioned all positive reactions to the tests were produced by the arsphenamines, while tests with the other arsenical preparations remained negative. This, however, does not account for the comparatively high percentage of positive reactions in the patients

who had never received any arsphenamine medication, many of whom had been treated with solution of potassium arsenite or some other arsenical preparation not of the arsphenamine series. As we have already shown, there was no evidence of specificity in the reactions to the different arsphenamines.

Epidermal Reactions as Compared with Other Types: It has been contended by some—especially by the proponents of the patch test—that since the severe forms of arsphenamine dermatitis, namely, the vesiculo-edematous-exfoliative varieties, seem to be preponderantly epidermal reactions, the patch test is better suited to detecting this type of hypersensitiveness than the intradermal test, and that the intradermal test may prove of more value for the vasculocutaneous types of reactions, such as urticarial and erythematous rashes, nitritoid crises and similar though milder reactions. On the other hand, Garnier, for example, found the intradermal tests consistently positive only in patients who had had a vesiculo-edematous dermatitis, and negative in 90 per cent of those who had had other types of rashes. Similarly, Clément Simon reported having made repeated intradermal tests on patients who reacted to the arsphenamines by nitritoid crises, headaches, diarrhea, etc., and found the reactions consistently negative.

In view of these conflicting results, it seemed worth while to report our results with the intradermal tests in patients whose intolerance to the arsphenamines manifested itself in symptoms not predominantly epidermal. Excluding, then, the patients in whom a severe exfoliative dermatitis (usually with vesiculation and edema) developed and including only those who had reacted to intravenous injections with rashes of the more immediate and ephemeral type (urticarial, erythematous) and also with nitritoid crises and similar but milder symptoms—in short, with reactions characterized by some writers as "anaphylactoid"—we found 19 patients in all, 5 of whom gave positive reactions to intradermal tests. This percentage is just about half that of the patients with dermatitis who gave positive reactions. There were 8 additional patients who suffered the so-called anaphylactoid reactions either before or after a severe exfoliative dermatitis. Seven of the 8 gave positive reactions to the intradermal tests; the eighth was tested only once. If one were to generalize from such small numbers, one might say that cutaneous hypersensitiveness can be demonstrated in approximately one half of the patients in whom a severe dermatitis develops without symptoms of any particular vasomotor instability, while the proportion rises to seven eighths among patients with dermatitis who have manifested such symptoms.

If the intradermal test did not show much agreement with clinical manifestations in the group of patients whose intolerance seemed to be

primarily of the vasomotor or anaphylactoid type, it at least showed a much higher percentage of positive reactions in patients with all types of intolerance than did the patch test.[2] Among the 52 patients who had, in all, 57 patch tests in addition to the intradermal tests, there were only 2 positive reactions to the patch tests (both in the same patient with dermatitis) as compared with 26 positive reactions to the intradermal tests. Among patients with dermatitis only, there were the 2 positive patch tests aforementioned, as compared with 15 positive reactions to the intradermal tests. The results of the two tests disagreed with each other in 24 of the 57 instances. It was not possible to tell whether the 2 positive reactions to the patch test were specific or not, as the patient was admitted to the clinic with an arsenic dermatitis after having been treated elsewhere, and a complete history was not obtainable.

The Test in Prognosis.—It is not sufficient that persons who have actually manifested intolerance to a given substance should give a positive reaction when tested with that substance. Of at least equal importance in therapeutics is the certainty or near certainty that persons who fail to react to a preliminary test injection of a drug will likewise tolerate that drug when it is administered in therapeutic doses, and conversely, that persons who react positively to a preliminary test injection will, in a large proportion of cases, manifest a more general intolerance to ordinary doses of the drug.

Syphilitic Patients Not Yet Treated with the Arsphenamines: We were handicapped in our experiments in this direction by a reluctance to perform intradermal tests on syphilitic patients who had not yet received any arsphenamine medication, as we feared that the test might sensitize them to the arsphenamine, thus making it impossible or at least inadvisable to give them the usual antisyphilitic treatment. However, we tested a small number admitted with syphilis—14 in all—who stated that they had not received any arsphenamine medication, although some had been given other arsenical preparations for various ailments. Three of these gave positive reactions to the tests; the remaining 11 showed negative reactions. One of the 3 who showed positive reactions was a patient with syphilis in whom jaundice had developed after he had received 18 injections of a special arsenical preparation not of the arsphenamine series. The tests performed during the jaundice were positive with all three arsphenamines in the standard dilutions. A second patient, with latent syphilis, admitted for lichen planus, gave positive reactions to all three arsphenamines, as did a third, a man

2. We used only old arsphenamine for the patch test, and consequently limited our comparison to results obtained with intradermal injections of this preparation. Since individual patients often had 15 or 20 intradermal injections apiece—sometimes more—we had to consider the limits of endurance of the person tested.

aged 62 with a primary lesion. For reasons not connected with the tests, it was considered inadvisable to give arsphenamine to any of these patients at that time. Of the 11 patients with syphilis as yet untreated with any arsphenamine who gave negative reactions to the intradermal tests, 2 were later treated with the aforementioned special preparation and did not receive any arsphenamine; 5 of the remaining 9 later tolerated treatment with arsphenamine without any complications, and 4 showed minor reactions only. One of these had what was interpreted as a Herxheimer reaction following the first injection of neoarsphenamine (0.3 Gm.), shortly after the test, but tolerated 43 more injections of neoarsphenamine without any reactions. A second patient reported diarrhea after the tenth injection of old arsphenamine, but tolerated three more courses of the same drug. A third had urticaria after the fourth injection of neoarsphenamine, but later injections caused no difficulty. The fourth patient, a woman, was occasionally nauseated after injections of old arsphenamine, but she was pregnant at the time. Obviously more tests need to be performed on patients with syphilis when they are first admitted, before any relationship between the outcome of an intradermal test and a subsequent reaction to arsphenamine medication can be established or disproved.

Syphilitic Patients Previously Tolerant of the Arsphenamines: There remains in theory the possibility that an intradermal test might be used to detect a latent or incipient intolerance in patients who have borne arsphenamine treatment without complications. When apparently tolerant patients who give positive reactions to an intradermal test shortly afterward show signs of intolerance, one may suspect that the patient's state of tolerance fluctuates, as local cutaneous hypersensitiveness has been shown to fluctuate, so that a positive reaction to a test may be an indication that medication should be stopped until the skin again gives a negative reaction, while a negative reaction to a test admits of continuation of the treatment.

We have already mentioned that of the 68 patients with syphilis who had not manifested any untoward effects from arsphenamine treatment up to the time of the first intradermal test, only 5 gave positive reactions to the test (3 of these reactions were weakly positive), and none of the 5 showed any untoward effects from subsequent intravenous injections. One had had 6 more injections of silver arsphenamine; another, 3 more of the same drug when last observed; the other 3 had not received any more arsphenamine. Three of the 5, when tested, had cutaneous eruptions apparently unrelated to arsenic medication; a fourth had vitiligo, and the fifth, pernicious anemia. Of the 63 who failed to react to the first test, all but 2 received further treatment with arsphenamine: 45 without any ill effects, and 16 with various symptoms of

intolerance, including dermatitis (3 cases), jaundice (5 cases) and neuritis (5 cases). The remaining reactions consisted of gastro-intestinal disturbances and transitory cutaneous rashes—chiefly urticarial.

Subsequent tests on these same patients, following their disturbances from arsphenamine therapy, continued to be negative, with 1 exception, a case of jaundice; in this instance a second test, done while the patient was still jaundiced, was negative, but 4 additional tests, several months apart, were positive. As the patient was not given any more arsphenamine on account of his hepatic condition, it was not possible to draw any inferences as to whether the positive cutaneous reactions indicated the development of another and possibly a different form of intolerance to the drug.

In short, since a considerable number of syphilitic patients previously tolerant of arsphenamine medication persistently gave negative reactions to the intradermal tests, but nevertheless later showed marked symptoms of intolerance to intravenous therapy, while the only patients in the tolerant group who gave positive reactions to the tests continued to tolerate the drug as before (barring, of course, the 3 patients not treated further), there seems to be little evidence to justify the test as an advance indicator of general or systemic intolerance in the course of arsphenamine therapy. It is of course possible that the reactors to the tests may show themselves to be reactors to treatment later on. It is also possible that those who failed to react to a first test but in whom nevertheless complications from subsequent arsphenamine therapy developed might have given some positive reactions if they had been tested at more frequent intervals before the onset of these complications. On the other hand, 2 patients in another group who happened to be tested within a few days prior to an outbreak of dermatitis gave negative reactions to the tests. The possibility that these patients were sensitized by the intradermal injections and that their dermatitis was a consequence of the test will be taken up separately.

SENSITIZATION AND DESENSITIZATION

Even though the intradermal test should prove itself of real value in the diagnosis and prognosis of complications from arsphenamine therapy, its practical usefulness would be greatly curtailed if it were shown that test injections even occasionally rendered patients hypersensitive to subsequent intravenous injections of arsphenamine. Experiments of some of the German investigators indicate that it is possible to sensitize both animals and human beings to the arsphenamines by intradermal injection of the drug in minute quantities. We therefore examined with special care the behavior of patients toward intravenous arsphen-

amine therapy after the tests, observing both general symptoms and any local recurrences or flare-ups at the sites of the tests. We also compared the reactions to later tests with earlier ones in cases in which the tests were repeated on the same patient.

The Test as a Sensitizer.—Reaction of Patients to Subsequent Intravenous Injections: We have already seen that of the syphilitic patients tested before receiving any arsphenamine, 1 gave a Herxheimer reaction following the first intravenous injection of 0.3 Gm. of neoarsphenamine on the afternoon of the test. This was the only instance in which a reaction of any kind was observed from an initial dose of arsphenamine in a patient who had previously been given an intradermal injection of the drug for purposes of testing. Among the patients already treated, but without any history of complications from treatment prior to the first test, there was not one who showed any reaction to the next intravenous injection after the test, the earliest reaction occurring after a third injection, or when 11 injections in all had been tolerated without any symptoms. Most of these patients had additional tests at various intervals after the first, and 3 of these, who were under treatment with arsphenamine at the time, received an intravenous injection an hour or so after the later test, without manifesting any symptoms. In the great majority of instances the patient had received in all several courses of treatment (all but 2 had had 19 or more injections) before giving any external symptoms of intolerance. This suggests a toxic phenomenon from the cumulative effects of the drug, rather than an allergic mechanism.

Outside the two groups just reviewed—namely, patients with syphilis not yet treated with arsphenamine and those treated without complications up to the first intradermal test—we found 6 additional patients in whom cutaneous manifestations developed from the next intravenous injection of arsphenamine given shortly after the test. It should be mentioned here that for the convenience of the persons tested, those who were being treated at the clinic were usually tested on the day on which they came for treatment; thus it frequently happened that a syphilitic patient would be given the intravenous injection of arsphenamine within an hour or so after the intradermal test injection. It would be surprising not to encounter more reactions to treatment in these patients, if the intradermal injection of the drug had any immediate sensitizing effect, and equally surprising not to meet with reactions to intravenous injections in cases in which an interval of from seven to ten days elapsed between the test and the next treatment, granting that an incubation period was necessary for the hypersensitiveness to develop, as in the classic anaphylactic syndrome.

We have summarized here the 6 cases in which symptoms of cutaneous intolerance followed the first intravenous injection of arsphenamine, which was given immediately (i. e., within from one to two hours) after the test:

CASE 62.—A white woman, aged 23, with secondary syphilis, received 5.2 Gm. of neoarsphenamine in 10 injections, following which generalized exfoliative dermatitis of twenty-four days' duration developed. After the skin had entirely cleared, seventy-seven days after the onset of the dermatitis, the first intradermal test with neoarsphenamine, and old and silver arsphenamine, in standard dilutions, was made. The reactions were negative. On the afternoon of the test, the patient received an intravenous injection of 0.2 Gm. of neoarsphenamine; this was followed the same evening by a recurrent dermatitis of two weeks' duration. A second intradermal test made during the recurrent dermatitis was also negative.

CASE 90.—A colored woman, aged 31, with florid secondary syphilis received 6.9 Gm. of neoarsphenamine in 15 injections. Inflammation of the eyes and edema of the ankles developed after the fifth injection. One week after the fifteenth injection, an intradermal test with the arsphenamines, in standard dilutions, was negative. An intravenous injection of 0.45 Gm. of neoarsphenamine was given on the afternoon of the test. On the following day an itchy eruption appeared on the hands, wrists and breasts and lasted about ten days. However, the next intravenous injection of 0.45 Gm. of neoarsphenamine seven days after the test did not cause any exacerbation of the dermatitis, and it is questionable whether the eruption was in any way connected with the arsenical preparations. No further tests were made.

CASE 93.—In a colored woman, aged 24, with latent syphilis, generalized urticaria, with pruritus and swelling of the face, developed after the fifth injection of old arsphenamine (making a total of 1.45 Gm.). The sixth dose was cut to 0.05 Gm. There was only itching of the feet after this dose. One week later an intradermal test, followed within half an hour by the seventh intravenous injection of old arsphenamine (0.05 Gm.), was made. Immediately after the intravenous injection there appeared a generalized eruption of urticaria with pruritus and profuse sweating; the throat was injected, and the tonsils were edematous. An intradermal test was negative. The patient received no further arsphenamine therapy, and no further tests were made.

CASE 104.—A white man, aged 22, with primary syphilis received 5 intravenous injections of silver arsphenamine which were tolerated without symptoms; headache and dizziness appeared in the evening after the sixth injection. Four days later, an intradermal test with the arsphenamines, in standard dilutions, was made. An intravenous injection of 0.2 Gm. of silver arsphenamine was given later in the same afternoon. Three days after this the patient returned with a maculopapular rash, chiefly on the trunk and extensor surfaces of the arms and thighs; the face was edematous. A diagnosis of arsenic dermatitis was made. On the next day, the sites of the intradermal tests showed cyanotic papules which lasted for two days. Under treatment with sodium thiosulphate the dermatitis cleared up in a little over a week. Eighteen days after the intradermal test and the last intravenous injection of arsphenamine, when the dermatitis had entirely cleared up, silver arsphenamine therapy was resumed, with 0.1 Gm. given intravenously. This was followed by a recurrence of the dermatitis, which persisted for about ten days, gradually clearing up under treatment with sodium

thiosulphate. Antisyphilitic therapy was continued with bismuth and mercury preparations in alternating courses. To a second intradermal test one year after the first the patient gave a more strongly positive reaction than before.

CASE 106.—A white man, aged 28, had florid secondary syphilis. Prior to the first intradermal test, he received 4.5 Gm. of neoarsphenamine in 10 injections. Vomiting and chills appeared after the fifth and tenth injections. An intradermal test three days after the last intravenous injection was negative for all three arsphenamines in standard dilutions. A patch test with old arsphenamine was negative. On the afternoon of the test, an intravenous injection of 0.3 Gm. of neoarsphenamine was followed by nausea, chills, general malaise and a scarlatiniform rash over the trunk and external aspect of the arms and thighs, lasting about three weeks. Six days after the injection there was an onset of jaundice. A second intradermal test, performed while the jaundice was still present but after the dermatitis had cleared, was negative. A third test nearly a year later produced a weakly positive reaction to old arsphenamine; the sites tested with neoarsphenamine and silver arsphenamine were negative. The patient received no more arsphenamine therapy, and no more tests were done.

CASE 215.—A white man, aged 40, with latent syphilis had generalized exfoliative dermatitis following medication with 4.2 Gm. of old arsphenamine in 8 injections. The first intradermal test, done during the dermatitis, was negative for all drugs in standard dilutions. Nearly three months later (two months after the dermatitis had cleared up) a second intradermal test was followed within an hour by an intravenous injection of 0.02 Gm. of silver arsphenamine. Five hours after this, a generalized scarlatiniform rash, accompanied by chills and fever, appeared. Three days later, all the sites of the second test showed a strongly positive reaction.

This case is of interest also in being the only one which showed a flaring up at earlier test sites on the subsequent injection of an arsphenamine. The sites of the first intradermal test injections, which had not shown reactions for three months became visible with the evolution of the dermatitis as pinkish-yellow papules, which persisted after the rash had almost cleared up and during generalized exfoliation.

The patient was not given any more arsphenamine, but his cutaneous hypersensitiveness was still in evidence almost a year and a half later, when a third intradermal test gave strongly positive reactions on all test sites, as did a fourth, fifth and sixth, performed at intervals of seven weeks, seven weeks and eight and one-half months, respectively. A seventh test four and one-half months after the sixth was positive for neoarsphenamine only.

In addition to these 6 cases, in which the intravenous injection followed the test immediately (i. e., within an hour), there were 5 others in which longer periods elapsed between the test and the next intravenous injection followed by cutaneous manifestations.

CASE 193.—A white man, aged 42, with syphilitic aortitis and tabes dorsalis, received 3 intravenous injections of old arsphenamine (0.2 Gm., 0.25 Gm. and 0.25 Gm.), at intervals of two weeks and one week, and intramuscular injections of a bismuth preparation on the same days. On the evening of the last injection, generalized urticaria with large wheals appeared and lasted for five days; it was accompanied by edema of the eyelids and ankles. The arsphenamine medication was stopped, and the injections of the bismuth preparation were continued. Three

weeks after the last injection of arsphenamine, an intradermal test was negative for all the arsphenamines, in dilutions of 1:100 to 1:20,000. Ten days after the test, an intravenous injection of 0.1 Gm. of old arsphenamine was followed the next day by generalized urticaria of three days' duration. Treatment was continued with bismuth and mercury preparations. No more arsphenamine was given, and no further tests were made.

CASE 244.—A white woman, 46 years of age, with latent syphilis, received a total of 0.3 Gm. of silver arsphenamine in three injections. The third injection was followed by nausea, flushing and fever. An intradermal test made one week later was negative for all the arsphenamines in standard dilutions. Two weeks after the test an intravenous injection of 0.05 Gm. of silver arsphenamine was followed by chills, headache, nausea and general malaise, and also by generalized pruritus, lasting about a week. The patient received no more arsphenamine, and no further tests were made.

CASE 28.—A white woman, aged 36, had congenital syphilis. Following the administration of 4.5 Gm. of neoarsphenamine in 9 injections, generalized exfoliative dermatitis of three and one-half months' duration appeared. Fifty-one days after the onset of the dermatitis, an intradermal test with the arsphenamines, in standard dilution, was negative. Mercury and bismuth preparations were given alternately during the next year, but no more arsphenamine. Fourteen months after the first intradermal test, a second test showed positive reactions to all three arsphenamines in standard dilutions; dilutions from 1:10,000 to 1:200,000 produced negative reactions. Five weeks after the second test, an intravenous injection of 0.05 Gm. of silver arsphenamine was followed the next day by plaques of dermatitis on the neck and cubital regions. The patient disappeared from observation.

CASE 198.—In a white man, aged 32, exfoliative dermatitis of four months' duration developed following 29 injections of neoarsphenamine for latent syphilis. The first intradermal test, eighteen days after the onset of the dermatitis, was negative for all the arsphenamines in standard dilutions. A second test, nine and one-half months later, was likewise negative. Six months after the second test, or about one year after the last intravenous injection, an intravenous injection (arsphenamine?) given by a local physician was followed within twenty-four hours by a generalized exanthem which lasted two weeks. Two and one-half months after the rash had cleared up, a third intradermal test was positive for silver arsphenamine only, in standard dilution. Other arsphenamines, including dilutions up to 1:200,000, produced negative reactions.

CASE 135.—In a Jew, aged 29, with secondary syphilis, dermatitis lasting four and one-half months developed after the administration of 4.7 Gm. of neoarsphenamine in 15 injections. Five months after this had cleared up the first intradermal test with all the arsphenamines in standard dilutions, was negative. A second test, five months after the first, was likewise negative. The patient received no more arsphenamine until a year after this second test, or more than two years after the last injection of neoarsphenamine, when a single intravenous injection of 0.05 Gm. of silver arsphenamine was followed within a few hours by a generalized scarlatiniform rash of two days' duration. No further tests were made. When last observed the patient was receiving sodium thiosulphate.

These 11 patients had already manifested some symptoms of intolerance to arsphenamine therapy before the first intradermal test. Seven of the 11 had had cutaneous rashes—5, exfoliative dermatitis, and 2, generalized urticaria—the others had reported headaches, dizziness,

nausea or vomiting. In spite of these symptoms, occurring both before and after the test, only 3 of the 11 gave positive reactions to the test which appeared to act as sensitizer, and in 1 of these the reaction was only weakly positive. A few additional patients showed minor symptoms, such as nausea, headaches and dizziness, from the first intravenous injection following the test, and a number of others had reactions of various kinds after tolerating without apparent ill effects the injections which followed closely the intradermal injections. However, all these patients had already manifested intolerance of one kind or another before they were tested, so it would be idle to assume that the tests were responsible post hoc. This needs to be taken into account particularly in cases in which a dermatitis has preceded the test, for it is not uncommon to see a recurrence of the dermatitis on the next attempt to administer arsphenamine intravenously, even in minute doses, to patients who have had no cutaneous tests of any kind.

Reaction of Patients to Repeated Intradermal Tests: If there is an allergic mechanism involved in abnormal reactions to arsphenamine, a patient's response to repeated intradermal injections of the drug should be of particular interest. Frei's experiments indicate that a considerable percentage of his laboratory animals (from 16 to 20 per cent in the case of guinea-pigs) could be markedly sensitized to neoarsphenamine by repeated intradermal injections of the drug, and that in about one half of the hypersensitive animals a local dermatitis developed on the test sites and on adjacent areas following the intracardial injection of neoarsphenamine. In further studies on patients seen at the clinic, Frei found that a first intradermal injection of neoarsphenamine sometimes produced a positive reaction ("Aufflammungsphänomen") at the site of the injection, which he considered a local serum sickness. On repeated intradermal injections into the same patients the reactions appeared earlier and were frequently accompanied by flare-ups at the site of the first injection. This was true mostly of patients as yet untreated with any of the arsphenamines.

Nathan and his co-workers found that on reinjection of sulpharsphenamine in patients without previous arsphenamine medication the reactions tended to appear earlier and to assume more of an urticarial character. Kaplun and Moreinis also noted an acceleration of the reaction time (from two to three days as compared with from seven to twenty-five days) on giving second intradermal injections of neoarsphenamine to patients who had given positive reactions to a first intradermal injection of the same drug. The later reactions were more intense than the earlier ones and were usually accompanied by flare-ups at the sites of previous injections. On the other hand, in 20 out of 24 of the persons tested by Kaplun and Moreinis who were given reinjections daily for

nine successive days the reaction remained negative; only 2 gave strongly positive reactions, accompanied by a flaring up at the sites of the previous tests, and 2 gave weakly positive reactions without any flare-ups at other sites. Chevallier reported that repeated intradermal injections of arsphenamine and other arsenical preparations produced reactions of diminished intensity and duration.

Some of these and other writers have reported cases of generalized exanthems following repeated intradermal tests, but it is not always clear whether the patients had already shown themselves to be reactors to the same drugs given intravenously. Lehner and Rajka noted malaise, chills, headaches and a rise in temperature from six to eight hours after later test injections of various substances, including neoarsphenamine. Following a series of second intradermal tests with sulpharsphenamine in patients not treated previously with arsphenamine, Nathan and Munk observed, in addition to numerous flare-ups at the sites of the earlier injections, 2 cases of a universal erythematous-urticarial exanthem in patients who had not shown a positive reaction to the earlier intradermal tests. A third test on 1 of these 2 patients resulted in an intense general reaction similar to the first, also with flare-ups at the sites of the earlier injections. A recurrence of a generalized arsphenamine dermatitis, lasting for a month, followed a second intradermal injection of neoarsphenamine two weeks after the first, in 1 of 6 cases of dermatitis studied by Puente and Cordiviola.

We never observed systemic reactions of any kind on repeating an intradermal test except in the cases already cited in which the patients had been given an intravenous injection in the meantime. It was in one of these cases (case 215) that we encountered the only instance of a flare-up at the sites of earlier injections on repetition of the test at a different location. As stated under "Types of Reactions," we observed some instances in which reactions to later tests appeared at shorter intervals than did reactions to the first test, and there were also a number of cases in which the later tests produced reactions of greater intensity than the earlier ones, but neither acceleration of the reaction time nor increased severity of the reactions occurred with any uniformity when we balanced the results for the entire series.

Arsphenamine Dermatitis as a Phenomenon of Sensitization.—The question whether arsphenamine dermatitis is an allergic or a toxic phenomenon is almost as old as the drug itself, and neither explanation alone suffices for more than a fraction of the number of cases reported. Since it is impossible to exclude the toxic effects of accumulated arsenic in cases of dermatitis occurring after lengthy treatment one must study the cases occurring after only a few injections, of small or moderate dosage, in order to judge the possible intervention of allergic factors.

Dermatitis After Few Injections and Small Doses: Of our total of 76 cases of dermatitis (exclusive of recurrences) definitely attributable to the arsphenamines, there were 18 in which the dermatitis occurred after from 3 to 6 injections, the total amounts ranging from 0.9 to 3.05 Gm. for neoarsphenamine, from 0.9 to 2.05 Gm. for old arsphenamine and from 0.5 to 1.50 Gm. for silver arsphenamine. Evidently, in the case of neoarsphenamine, a dermatitis may be provoked by an amount no larger than that frequently administered by some clinicians in a single injection. Eleven, or approximately 62 per cent, of these patients gave positive reactions to 1 or more intradermal tests—a higher proportion than that encountered in any other major group. In 9 additional instances, there was a recurrence of a previous dermatitis from the injection of a single minimal dose of arsphenamine after intervals ranging for the most part from several months to a year or more without any arsenic medication. In 4 of these cases the same arsphenamine as that which had provoked the first eruption was given; in 4 cases a different preparation of arsphenamine was used; in 1 case the injection causing the recurrent dermatitis was administered by a physician outside the clinic, and the preparation was recorded merely as "salvarsan." Some of these cases represent attempts at desensitization and will be further discussed under that topic.

Polyvalent Sensitization: The question has often been raised whether sensitization to one substance can render a person hypersensitive to other substances of different composition. Among the persons tested we saw several instances in which cutaneous hypersensitiveness to arsphenamine appeared to carry in its wake symptoms of intolerance to other substances previously borne without ill effects. We also saw several cases in which an acute exfoliative dermatitis seemed to pass over into a chronic eczema, with remissions and exacerbations whose exciting factor we were unable to discover. Following are brief summaries of the cases of multiple or polyvalent hypersensitiveness in which definite substances were incriminated.

CASE 97.—A Jewish housewife, aged 38, had latent syphilis. Following 8 injections of arsphenamine and 15 injections of a bismuth preparation at another clinic, the patient broke out with an eruption which started behind the ears and gradually spread over the scalp, neck, chest, axillae, abdomen and genitocrural folds, in the order named. On admission of the patient to the Vanderbilt Clinic the regions involved were covered with patches of reddish, dry, eczematoid dermatitis. This condition cleared up slowly under treatment with sodium thiosulphate, but recurred after the patient used a hair dye containing paraphenylenediamine. She admitted having used this dye for several years, but could recall no previous instance of a rash following its application. The condition again improved under treatment with sodium thiosulphate, but grew worse immediately after a shampoo. A third recurrence followed an application of cold cream. Samples of the soap and cream for testing have not yet been obtained.

Meanwhile the patient had received several intramuscular injections of mercuric salicylate. Patch tests were negative for old arsphenamine, neoarsphenamine, mercuric salicylate, a bismuth preparation and paraphenylenediamine, but a second patch test with paraphenylenediamine was strongly positive. Intradermal tests with the arsphenamines were negative on three separate occasions. The patient remained under observation.

CASE 170.—A Greek milliner, aged 21, received 16 intravenous injections of neoarsphenamine for primary syphilis. Following these injections patches of red, oozing dermatitis developed on the forehead, eyelids and scalp. The lesions spread to the neck, chest and arms. Similar lesions appeared on the soles. The condition improved under treatment with sodium thiosulphate and afenil, and later with gentian violet, but frequent exacerbations occurred during the following months. These were traced to dyed materials used for hats and clothing. The patch tests with paraphenylenediamine were positive; those with old arsphenamine, negative. Intradermal tests with neoarsphenamine and old and silver arsphenamine were negative four times in succession. There was no history of rashes prior to the arsphenamine dermatitis, although the patient had worked as a milliner for several years.

CASE 131.—A German porter, aged 48, had received about 80 "hip injections" (mercury preparation?) for syphilis eighteen years before this report. There was no record of cutaneous eruptions of any kind. Two years before this report, on the appearance of general symptoms he received from a local physician 14 intravenous injections and about 24 intramuscular injections.

Generalized oozing dermatitis appeared after the last intravenous injection and lasted from six to eight weeks. About ten days before the patient's admission to this clinic another local physician had given him two inunctions with a bluish ointment (mercury preparation?) on the thighs and abdomen, after which an erythematopapular and pustular eruption developed on the scalp and neck and in the axillae, cubital regions and genitocrural folds; similar but discrete lesions appeared on the abdomen. The diagnosis of the admitting physician was "mercurial dermatitis." This cleared up under injections of sodium thiosulphate, but after intramuscular injections of a bismuth preparation an erythematous rash, with intense pruritus, appeared over the entire trunk. Four months later, the patient was given 5 more injections of a bismuth preparation (1 intravenously and 4 intramuscularly), and a stomatitis developed. After an interval of three months, a bismuth preparation was again tried. The eighth injection was followed by a new rash over the chest, arms and crural regions. Treatment by mouth with tablets containing mercury and potassium iodide brought on gastro-intestinal symptoms and fresh patches of eruption on the legs. Another generalized rash appeared after the patient had used a new soap mixture to clean the office. Intradermal tests with the arsphenamines were positive on 3 separate occasions.

In cases like the last one, in which a patient who is intolerant of an arsphenamine shortly afterward shows symptoms of intolerance to bismuth or mercury preparations, it is well to consider the possibility that the apparent hypersensitiveness to these preparations may be due to minute amounts of arsphenamine retained in imperfectly sterilized syringes used for both kinds of injections. Schoch has presented convincing evidence that in some cases of marked hypersensitiveness to arsphenamine the almost infinitesimal amount received in this way can cause a severe recurrence of symptoms.

Rôle of Paravenous Infiltration: The rôle of paravenous infiltration in bringing on arsphenamine dermatitis is still a moot question. Such infiltration would seem to afford an excellent opportunity for cutaneous sensitization. Of the 5 cases known and recorded among the group under investigation here, 1 occurred two months after the dermatitis and did not bring about a recurrence of the dermatitis. In 2 other cases paraphlebitis was still in evidence ten days and three weeks after the infiltrating injection, but no generalized dermatitis developed, although both patients remained under treatment for more than a year afterward. In the fourth case, a dermatitis appeared about eighteen days after the infiltration; this patient had received 5 more intravenous injections in the interval, without symptoms. In the fifth case the dermatitis appeared in the cubital folds within five days after the infiltrating injection and became generalized during the next few days. General conclusions, however, are hazardous, for it is almost certain that in any large clinic, in which injections are given by nurses and sometimes by students, more paravenous infiltrations occur than are recorded, even with the most careful supervision. And it must be admitted that in the private practice of one of us (Dr. Cannon), in which all injections are given by the physician personally, not a single case of generalized exfoliative dermatitis has been encountered over a period extending well into the second decade.

Desensitization.—Protective Action of Previous Arsphenamine Medication: From certain findings recorded in previous sections of this article, we have seen that a theory of sensitization might explain a considerable proportion of cases of arsphenamine dermatitis which it would be difficult to ascribe to arsenic poisoning alone. Why, then, should we encounter so many discrepancies between the patients' response to arsphenamines introduced intravenously and their reaction to the same preparations injected into the skin, the supposedly sensitized organ? Why did intradermal injections of the arsphenamines give so little evidence of initiating a state of hypersensitiveness in patients who had not had any cutaneous manifestations attributable to preparations of this series? Reasons for the difference between our results and those of the investigators cited may lie at least partly in the fact that the persons tested by us comprised a larger number of patients already treated with the arsphenamines. We have already suggested that the smaller percentage of positive cutaneous reactions which we observed in patients treated with arsphenamine as compared with those who had never received arsphenamine (30.7 per cent as compared with 45.8 per cent) might be due to some protective or desensitizing effect from the intravenous medication. In fact, Kaplun and Moreinis were emphatic in stating that in no case in which a patient had received or was receiv-

ing treatment with arsphenamine (32 cases) did an intradermal injection produce a positive reaction. Similarly, Frei appears to have found his "Aufflammungsphänomen" consistently absent in patients treated with arsphenamine (77 cases), with the single exception of his case of dermatitis, reported in a previous article. On the other hand, the positive reactions reported by Garnier all occurred in patients treated with arsphenamine (only those who had a vesiculo-edematous dermatitis showed consistently positive reactions), while his 25 control persons who had never received neoarsphenamine always gave negative reactions to intradermal injections of this drug, even when the injections were repeated several times.

The 16 untreated persons tested in the Stuart and Maynard series all gave negative reactions to intradermal injections of old arsphenamine and neoarsphenamine, while the only positive reactions occurred in 2 patients who had had arsphenamine dermatitis of the severe exfoliative type. The danger of generalizing from a limited number of examples is illustrated also in our own recent experience with a group of patients in whom abnormalities of pigmentation developed—some following arsphenamine dermatitis and others apparently from retention of arsenic of unknown origin. In this group of 10 persons, we found intradermal tests with the arsphenamines consistently positive. When these patients were later reexamined in conjunction with nearly 250 additional ones, the picture assumed a different perspective.

If previous arsphenamine therapy—up to the point where it ceases to be tolerated—does exercise a protective influence against sensitization by intradermal injection, we should expect to see a difference between cases in which the treatment has been recent and those in which long intervals—several months or years—have elapsed between the last treatment with arsphenamine and the test. As a matter of fact, we did find that the majority of positive tests occurred in patients whose last medication with arsphenamine dated from a fairly long time before the test was made, much longer, on the average, than in the cases in which the tests were negative. One must take into account, however, that the longer intervals were often occasioned by some serious complication, such as a dermatitis, jaundice or neuritis, so that this may mean little in itself.

Desensitizing Effect of Intravenous Injections Immediately Following Intradermal Injection: Kaplun and Moreinis, and also Sulzberger, found that if guinea-pigs were given intracardial injections of arsphenamine within twenty-four hours after a first (sensitizing) intradermal injection of the drug, reactions from subsequent intradermal injections were forestalled. If the intracardial injections were given at longer intervals after the first or sensitizing intradermal injection, they did not exercise any preventive action. This suggests that the comparative infre-

quency of symptoms of sensitization in our patients after the tests may have been due partly to our custom of giving the person tested (if syphilitic) an intravenous injection on the same afternoon as the test.

In all these studies and in similar ones involving patients treated with arsphenamine and untreated patients, there is, of course, the question whether the differences in results may not be due to the syphilis rather than to the arsphenamine. It is rather interesting to recall that in a series of intradermal tests with serum only, Biberstein and Oschinski obtained far fewer positive reactions in patients with syphilis than in normal persons.

TABLE 2.—*Recurrent Dermatitis After a Single Minimal Dose of Arsphenamine*

	Preparation and Amount Responsible for Recurrent Dermatitis			Preparation and Amount Responsible for the First Dermatitis		
Case	Amount, Gm.	Preparation	Interval Between This and the Last Injection	Amount, Gm.	Preparation	Injections
215	0.02	Silver arsphenamine	2⅔ months	4.2	Old arsphenamine	8
135	0.05	Silver arsphenamine	2 years	4.7	Neoarsphenamine	15
28	0.05	Silver arsphenamine	1 year and 2 months	4.5	Neoarsphenamine	9
104	0.1	Silver arsphenamine	2 weeks and 4 days	1.3	Silver arsphenamine	7
179	0.1	Silver arsphenamine	3 months	3.05	Neoarsphenamine	6
214	0.1	Silver arsphenamine	2 weeks	0.8	Silver arsphenamine	4
62	0.2	Neoarsphenamine	2⅔ months	5.2	Neoarsphenamine	10
198	? †		1 year and 1-2 months	?	Neoarsphenamine	29
12	Provocative injection	Neoarsphenamine	4 months	? †	"Salvarsan"	8
				? †	Neoarsphenamine	10

† Given by a physician outside the clinic.

Clinical Attempts at Desensitization: In cases of manifest intolerance of arsphenamine one naturally seeks a remedy which will not deprive the patient of the benefits of antisyphilitic treatment. Mercury and bismuth preparations, while valuable as adjuvants, are not satisfactory substitutes for arsphenamine over long periods. A change from one arsphenamine to a different preparation of the series will sometimes solve the problem. A considerable number of our patients who were unable to tolerate neoarsphenamine did well with old arsphenamine, and some who reacted badly to both of these preparations later tolerated silver arsphenamine. However, we have already seen that in some patients a recurrent dermatitis developed when treatment was resumed with a different arsphenamine from that which had caused the original dermatitis. Especially when the patient's intolerance is suspected of being a phenomenon of sensitization, it seems logical to attempt desensi-

tization by recommencing treatment with very small doses of the drug at frequent intervals and increasing them gradually until the normal level is again reached.

Practically all of our cases in which treatment with arsphenamine was resumed after the patients had suffered serious complications from previous treatment represent attempts at desensitization by this method. That these attempts were not uniformly successful has already been intimated in connection with the 9 cases in which patients who had had one attack of dermatitis suffered a recurrence after a single small dose of arsphenamine. These cases are summarized in table 2.

The cases listed in the table were for the most part cases of severe exfoliative dermatitis lasting from several weeks to several months; 2 were milder and cleared up in one week and ten days, respectively. The recurrences were of various types; some were erythematous and lasted only a few days, and others reproduced the original severe symptoms of vesiculation and edema, with subsequent exfoliation. A third attempt at arsphenamine therapy was made in 2 of these patients: One patient (case 12) had received 0.85 Gm. of old arsphenamine in 4 injections, with only slight nausea, when last seen; the other (case 179) later tolerated a total of 0.9 Gm. of old arsphenamine in 8 injections, beginning with 0.05 Gm. and not exceeding 0.15 Gm. in a single dose; there were itching and nausea after the sixth injection only.

In 3 other cases, "desensitization" dosage appeared to be successful for a time, but rashes eventually developed after the patients had received a number of injections:

Case 166.—In a Swedish girl, aged 18, a dancer, with secondary syphilis, a dermatitis developed after 6 injections of neoarsphenamine, totaling 2.6 Gm. After an interval of one year, during which 26 injections of a bismuth preparation failed to reduce a positive Wassermann reaction, treatment with arsenic was cautiously resumed, beginning with 0.025 Gm. of silver arsphenamine and increasing gradually, at weekly intervals, as follows: 0.025, 0.05, 0.075, 0.075, 0.1, 0.075, 0.1, 0.15, 0.15, 0.2, 0.2 and 0.2 Gm. Headache and slight malaise appeared after the first injection. The next 9 injections were well tolerated. After the eleventh injection (0.2 Gm.) reddish plaques of seborrhea-like dermatitis appeared on the neck, arms and thighs, but the attending physician did not attribute this to the medication, and gave the twelfth injection of 0.2 Gm. The dermatitis became definitely worse, with pruritus; the duration was about one month altogether. The Wassermann reaction was still positive at this time, but became negative during the next course of treatment with a bismuth preparation. No more arsphenamine was administered.

Case 199.—A colored domestic, aged 39, had latent syphilis. Four months after a dermatitis from neoarsphenamine, therapy was resumed with silver arsphenamine. After 3 injections (0.05, 0.15 and 0.25 Gm.) a rash broke out. The attending physician did not attribute this to the medication, and gave 5 more injections of 0.3 Gm. each. By this time the patient had an eruption resembling erythema multiforme around the left eye, with edema of the lids, similar patches, from

the size of a dime to that of a dollar, over the hips and thighs and a vesicular eruption on the palms; there was generalized pruritus. The symptoms cleared up under medication with sodium thiosulphate, and antisyphilitic treatment was continued with a bismuth preparation.

CASE 247.—In a colored domestic, aged 42, with latent syphilis, a moist maculopapular pruritic eruption appeared on the extensor surfaces of the forearms, axillae and internal aspect of the thighs following 8 injections of old arsphenamine (a total of 1.70 Gm.). Arsphenamine was discontinued, and sodium thiosulphate was given intravenously. Two weeks later only pigmented spots remained. After an interval of five months during which the patient received 10 intramuscular injections of a mercury preparation, silver arsphenamine was tried, beginning with 0.1 Gm. This was followed within an hour by a marked urticaria. The next 2 doses were reduced to 0.05 Gm. each, and 1 cc. of epinephrine was given fifteen minutes before the arsphenamine. Since these were well tolerated, the third dose was raised to 0.1 Gm., with 0.25 cc. of epinephrine preceding it. Immediately after the injection, urticaria with large wheals appeared over the body. The drug was then changed to neoarsphenamine, and 5 injections were given (0.05, 0.1, 0.15, 0.15 and 0.15 Gm.) each preceded by 0.5 cc. of epinephrine. After the last injection, chills, pains in the joints and soreness in the epigastrium developed. Neoarsphenamine was discontinued, and for the next two months the patient was given weekly injections of sodium thiosulphate. About three months after the last administration of neoarsphenamine treatment was resumed with the same drug. The first injection was of 0.05 Gm. preceded by 0.5 cc. of epinephrine. On her next visit, the patient reported that five hours after this injection she had had chills, fever and suffusion of the eyes, lasting all night. Red spots had appeared over the body, with intense itching, and lasted for several days. After an interval of two weeks, 0.05 Gm. of neoarsphenamine was again tried, preceded by 0.5 cc. of epinephrine as before. A third dose similar to the preceding, after a four weeks' lapse, was followed in about three hours by chills, hot flushes, nausea and weakness. Two weeks later, however, the dose was increased, first to 0.1 Gm. and then to 0.15 and 0.2 Gm., still with epinephrine, until a total of 1.70 Gm. had been given, in 14 injections. The Wassermann reaction, which had become negative under the first course of treatment (old arsphenamine) remained negative, and the patient was receiving a mercury preparation when last observed.

Another case of recurrent urticaria after a number of injections of greatly reduced dosage has already been summarized (case 193).

It is possible that if some of these attempts had been carried out further, in spite of recurrent symptoms of intolerance, we might have achieved more positive end-results. It is also regrettable that such long intervals frequently elapsed between the injections. We gained the impression that our best results in "desensitization" therapy were secured when we were able to give the patient very small doses closely spaced for the first few injections on resuming treatment after a dermatitis; but it is exceedingly difficult to manage this when dealing with outpatients in a large city clinic, and we have not yet had sufficient opportunities to demonstrate whether fractional doses at still shorter intervals would prevent all recurrent eruptions following the first injection of the new course.

COMMENT

Further studies in excretion of arsenic and in the passive transfer of hypersensitiveness to arsphenamine, on which we are now engaged, may bring to light additional relationships between toxic and allergic manifestations due to arsphenamine. What we have seen already leads us to believe that the two processes are not as mutually exclusive as has generally been assumed. Under normal conditions there is evidently a rhythmic ebb and flow of ingested arsenic from the organs of storage into the blood stream and vice versa, only a fraction at a time being definitively lost through the excretory organs. There is not much question but that the skin participates in this ebb and flow—in fact, the varying amounts of arsenic we have found in specimens of skin from the same patient analyzed at different times offer concrete evidence of this. The internal release of stored arsenic into the blood stream could thus produce in the skin successive small-scale sensitizations (Zieler), which would remain subclinical so long as the skin's local powers of adaptation were adequate to metabolize its quota of the substance. As this quota was exceeded, either through retarded excretion or limitations in cutaneous reactivity, we should then see the outbreak of a clinical dermatitis. To call this an arsenic poisoning when it occurs after 5 Gm. of arsphenamine, and a phenomenon of sensitization when the same picture appears after one tenth of that amount, may prove to be as artificial a distinction as to say that a man who drowns in the Atlantic Ocean and one who drowns in a bathtub die from different causes.

In ordinary experience one sees only an occasional person who is hypersensitive to primroses. Bloch, however, succeeded in sensitizing to primroses 100 per cent of the persons he tested by using concentrated extracts or repeated applications and (or) by abrading the skin of otherwise refractory subjects. When Biberstein and Oschinski failed to produce symptoms of sensitization in persons tested by intradermal injection of 0.1 cc. of serums from other species, they found that increasing the amount or repeating the injections produced positive results. All workers who constantly handle nickel salts sooner or later develop nickel eczema. In all these examples, the idiosyncratic person is merely one whose hypersensitiveness crops out earlier, or after a lesser stimulus, than the average. It appears more and more to be a matter of degree, rather than of kind.

One might safely say that there are as many different thresholds of tolerance for a given medicament as there are individuals of the species; only the differences in the majority of cases are so slight as to enable us to use a therapeutic index as a fairly safe guide to dosage. Actually, of course, the standard therapeutic dose does not necessarily coincide with the optimum for any individual patient, just as the standard toxic

dose may not coincide with the limit of tolerance of any single person. Add to this the functional variations of the person at different times and under different conditions, and it is not difficult to see that with just a slight shift in the balance, what we have termed a subclinical sensitization may at any time become a clinical dermatitis.

Previous investigations and others under way indicate that patients with arsphenamine dermatitis show a tendency to a delayed excretion of arsenic. This does not necessarily mean that the process of sensitization is nothing more or less than arsenic poisoning. With the perfecting of newer methods of chemical analysis, doubtless many intermediate products of the original arsphenamine molecule can be traced in the tissues and body fluids, while now we are chiefly dependent on the identification of the arsenic component when we attempt to follow the course of successive accumulations and eliminations of the drug. When we speak of a patient as "tolerating" arsphenamine, it would not be unreasonable to conceive of this as an automatic desensitization, whereby the cells of the skin—to confine ourselves to the problem of dermatitis—learn to transform increasingly large amounts of arsphenamine brought by the blood stream, both directly (by injection) and intermittently from various internal storage depots. The cumulative action of the drug, instead of being separate and distinct from its sensitizing action, as is usually assumed, would thus constitute with this a single process. A patient would tolerate arsphenamine as long as the rate of accumulation or sensitization in any tissue did not exceed the rate of metabolism or desensitization within that tissue. This could be accomplished by means of an antigen-antibody reaction, the antibody constituting a normal product of metabolism. An excess of antibody is postulated for serum sickness and other manifestations of hypersensitiveness. Dermatitis may likewise result from an excessive production of antibody in an effort to cope with increased retention of antigen—in this case, arsphenamine or its by-products. Hence the importance, generally recognized in practice, of alternating courses of arsphenamine with courses of bismuth or mercury medication.

The intradermal injection of arsphenamine, even in high dilutions, represents a sudden introduction into the dermis of an amount of antigen much greater than that which would reach that area at any given moment by way of the blood stream. Whether this results in a positive local reaction or not could conceivably depend solely on the person's ability to manufacture an excess of antibody in situ and would not necessarily parallel his response to intravenous injections, when the substance is distributed to all parts of the organism, correspondingly diluted and probably changed en route. This is particularly applicable to cases of positive reactions in clinically tolerant patients. In the case of negative

reactions in patients with dermatitis, it is not surprising that areas of skin refractory to the dermatitis (the ones usually sought out for the test) should also prove refractory to intradermal injections. What part nerve endings play in these local differences, as suggested by Milian, is still a matter of conjecture, but our exceptionally high percentage of positive reactions in patients with dermatitis who had also manifested symptoms of vasomotor instability, suggests that some positive reactions, at least, represent a toxic sensitization complicated by vasomotor disturbances.

Our experience with various dilutions of the arsphenamines, as used in the intradermal tests, seems to bear out the theory of the quantitative nature of the reaction. If it is at all analogous to the experiments of Bloch with primrose, then all persons could be sensitized by way of the skin—or at least made to give "positive" reactions—by using sufficiently strong concentrations or repeating the injections. Desensitization may be a matter of finding out what infinitesimal amount of the antigen can be introduced to enable the tissues to keep pace in the formation of antibodies without producing in excess. Castoldi's intradermal tests on patients who had had arsphenamine dermatitis are interesting in this connection. He began by injecting 0.05 cc. of arsphenamine, in dilutions of 1 : 10,000, and when the sites gave 2 negative reactions in succession, he further repeated the tests with dilutions of 1 : 1,000 and then 1 : 100. Although he continued his experiments on the same patients over a period of several months, he never obtained a positive reaction. As a diagnostic test this was a failure, and he so construed it, but actually he may have achieved a desensitization. We have not as yet made any parallel experiments, but the point merits further study for its practical possibilities. Similarly, when one is obliged to interrupt antisyphilitic treatment, either as a precaution after minor symptoms of intolerance or because of an acute dermatitis, it would be desirable to attempt desensitization by resuming intravenous injections with minute doses, at shorter intervals than we have for the most part been able to employ heretofore, and increasing the dosage very gradually, guided by the response of each patient rather than by the theoretic standard of what he ought to be able to tolerate.

SUMMARY

1. This series of experiments, comprising 1,586 test injections in 256 persons, failed to show any constant relationship between the reactions to the intradermal test and the clinical reactions of these persons to arsphenamine therapy.

2. The test gave positive reactions in 48.7 per cent of the patients who had had arsphenamine dermatitis—a higher percentage than in any other major group, but not high enough for practical purposes.

3. The test is lacking in specificity, and hence is of little or no diagnostic value, for the following reasons:

(*a*) Only 5 of 76 patients with dermatitis reacted positively to test injections of the arsphenamine which caused the dermatitis and negatively to other arsphenamines, while some patients gave no reaction to test injections of the arsphenamine which caused the dermatitis but gave positive reactions to tests with other arsphenamines.

(*b*) The test was positive in patients who presented eruptions from medication with other arsenic compounds but who had never received arsphenamine.

(*c*) It was repeatedly negative in patients known to have complications due to arsphenamine.

4. The test is of little or no prognostic value, for a considerable number of syphilitic patients previously tolerant of arsphenamine medication persistently gave negative reactions to the tests, but nevertheless later showed marked symptoms of intolerance of intravenous therapy, while the only patients in the tolerant group who gave positive reactions and were treated further continued to tolerate the drug as before.

5. We found no proof of any patient's having been sensitized by an intradermal injection of arsphenamine. Various facts indicate that intravenous injections, either before or immediately following intradermal injection, protect against sensitization by the cutaneous route.

6. Arsphenamine dermatitis as a phenomenon of sensitization may not differ essentially from arsphenamine dermatitis as a toxic manifestation.

7. Desensitization, successful in some cases recorded here, deserves further trial.

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ABSTRACT OF DISCUSSION

DR. JOSEPH V. KLAUDER, Philadelphia: I think that Dr. Cannon's observations agree with the work of Frei and Sulzberger concerning the sensitization of guinea-pigs to arsenic and with my observation of a patient who apparently became sensitized to arsphenamine after intracutaneous injections and in whom asthma and eczema developed later after exposure to arsphenamine. I hope that we shall be able to determine from Dr. Cannon's study, which I understand

is not yet completed, when it is safe to resume administration of the arsphenamines after the occurrence of arsphenamine dermatitis.

Dr. Cannon's study suggests the possibility of desensitizing a patient who is intolerant of the arsphenamines. This recalls the method which exists in some places of giving initial injections of very small doses of arsphenamine in an endeavor to prevent reactions to much larger doses. I believe that it is generally recognized that infiltration of the tissues through a faulty venipuncture is hazardous, as it frequently results in sensitizing the patient to arsenic and enhances the possibility of arsphenamine dermatitis appearing after subsequent injections of arsphenamine. In a recent personal conversation with Frei, he assented to the truth of this possibility.

After the tissues become infiltrated with arsphenamine, one is at a loss to know whether to continue the administration of the drug, or to interrupt its use in order to avoid arsphenamine dermatitis when the drug is again given. Frei believes that the administration of the drug should be continued and not interrupted. It is possible that Dr. Cannon's study will furnish information regarding this important question.

Dr. John H. Stokes, Philadelphia: I believe that I have seen some evidence that sensitiveness to an arsphenamine derivative may be induced by patch testing conducted as a routine on patients who have never received the drug. An incidence of 3 cases of dermatitis in 100 injections under such patch testing decreased, perhaps merely coincidentally, to no cases in the next 1,000 injections without patch testing. The question as to whether the epidermis is thus permeable to an arsenical preparation is now under experimental study. It is worth while, too, to recall the possible nonspecificity of cutaneous tests with irritants and with necrotizing substances. If necrosis is produced, pseudopositive adsorption reactions may occur, even with high dilutions. The atopic state, too, may give rise to an excessive tendency to a positive reaction, as Moore, Wu and Robinson have shown. In the injection of irritants into the skin, cyclic or periodic reactivation at the site of infection can be observed, as occurs with insect bites, the use of formaldehyde, etc., and these may perhaps confuse a positive picture. The influence of the general state of the person as affected by environment, diet, etc., probably modifies the interpretations, as Sulzberger, for example, has shown.

Dr. A. Benson Cannon, New York: I wish to thank Dr. Klauder and Dr. Stokes for discussing my paper. As Dr. Klauder has shown, it really is possible to desensitize a person after arsphenamine dermatitis. Formerly, I was of the opinion that any patient who had had a generalized exfoliative dermatitis from one of the arsphenamines would always be intolerant of subsequent injections of that particular drug. A number of years ago, together with Dr. Fordyce in consultation with another physician, I saw a case of arsphenamine dermatitis, and although the patient had a most severe type of dermatitis with universal redness, vesiculation, crusting and swelling, with fluid in the chest, and albumin and casts in the urine, he made an excellent recovery. About a year later, he came to the office to see Dr. Fordyce, and I was astounded to hear that he had been given 8 more injections of the same arsphenamine that had caused the dermatitis in the first instance, without the slightest reaction. The man was found to have neurosyphilis, and I, too, gave him from 25 to 30 injections of arsphenamine as well as a number of intraspinal injections without his exhibiting any evidence of intolerance of the drug. This case is, of course, unusual, but we do see patients with a definite arsphenamine dermatitis who subsequently are able to tolerate another arsphenamine and sometimes the same drug if it is cautiously administered, begin-

ning with very small doses of 0.07 or 0.05 Gm. at intervals of from a week to ten or twelve days and gradually increasing the dose. While there may be a slight flare-up of the dermatitis with the first few injections, such reactions have a tendency to subside rapidly, and the patient becomes tolerant of succeeding injections in fairly large doses.

I thought that Dr. Stokes' observations on the occurrence of a dermatitis after patch tests with the use of arsphenamines were interesting. We had only 3 patients who had never received arsphenamine but who gave strongly positive reactions to arsphenamine with the patch tests and in whom a generalized dermatitis subsequently developed following treatment with arsphenamine. I think that it is necessary to study a large series of cases before one can determine whether tests with the arsphenamines render a patient sensitive to intravenous treatment with the drug. In the beginning of our investigation we too had much difficulty in interpreting the cutaneous reactions obtained with intracutaneous and patch tests with the arsphenamines. By carefully controlling each test and using suitable dilutions, we think that we can fairly satisfactorily diagnose a positive cutaneous test with the drugs used.

EPIDERMOMYCOSIS AT THE UNIVERSITY OF CALIFORNIA

STUDY IV.

ROBERT LEGGE, M.D.

LEE BONAR, PH.D.

AND

H. J. TEMPLETON, M.D.

OAKLAND, CALIF.

In our studies of epidermomycosis we treated groups of students with various remedies of known or supposed value. The students in the groups were observed at weekly intervals, and their progress or lack of progress was recorded. The type of the infection was labeled as interdigital, vesicular, squamous or eczematoid, and the degree of severity was judged by a scale ranging from plus one to plus four. In order to make the grading as accurate as possible, all of the examinations were made by a trained personnel.

STUDIES OF THERAPEUTIC RESULTS IN 1929

In 1929, our first year, we made the mistake of attempting to study too many remedies, with groups of students that were too small in number. Although our groups were sufficiently large at the beginning of the semester, at the end of the term we had too few students who had completed the treatment.

Groups of students varying in number from twenty-one to six completed an adequate treatment with the following preparations: 30 per cent sulphurous acid in glycerine; 1 per cent thymol in glycerin, 10 per cent aqueous "lime sulphur" compound, Castellani's solution,[1] 10 per cent ointment of benzyl peroxide, tincture of iodine and glycerin in equal parts, 10 per cent solution of sodium thiosulphate, Whitfield's ointment, Whitfield's ointment containing 1.25 per cent thymol, 4 per cent chrysarobin in chloroform, a pine oil soap solution, 5 per cent gentian violet in alcohol, 5 per cent aqueous solution of mercurochrome and 10 per cent ointment of copper oleate.

From the Cowell Memorial Hospital and the Department of Botany, University of California. This work was made possible by grants from the Research Fund and from the Associated Students of the University of California.

1. This solution is composed of 10 per cent basic fuchsin containing 5 per cent phenol, to which is added: boric acid, 1 per cent; acetone, 5 per cent, and resorcinol, 10 per cent (Castellani, Aldo: Treatment of Certain Types of Epidermophytosis by Means of a Carbol-Fuchsin Test, New Orleans M. & S. J. **80**:833, 1928).

Sulphur in the form of a 30 per cent sulphurous acid in glycerin showed a sufficiently high percentage of total satisfactory results (42.8) to cause us to try it again in 1930 on a larger series of patients. A drawback to its use in this form was the rather high percentage (9.5) of patients whose skins were irritated by it. In the form of a solution of sulphurated lime, such as is used by agriculturists in spraying plants, it brought about 44.4 per cent of satisfactory results.

Whitfield's ointment worked satisfactorily on 38.4 per cent of the patients on whom it was tried, and in another group, when 1.25 per cent of thymol was incorporated in it, the satisfactory results increased to 58 per cent. The latter group, however, also showed the highest percentage (10.6) of irritation.

Our highest percentage of satisfactory results (65) was found in the group treated with iodine.

Although thymol seemed to increase the effectiveness of Whitfield's ointment, when used alone in acetone it was not particularly effective.

Castellani's solution was tried and found statistically satisfactory, but it was abandoned because of the clinical impression that it produced too much dryness and fissuring. The same statement holds true for gentian violet.

Although mercurochrome gave a high percentage of satisfactory results (62.5), our clinical experience with it in private practice did not encourage us to try it further.

Because of unimpressive results or small series of cases the other remedies in this series were not tried further.

Summary.—Compounds of sulphur, iodine, Whitfield's ointment and Whitfield's ointment plus thymol were tried on sufficiently large groups of students and with enough success to warrant further trial.

STUDIES OF THERAPEUTIC RESULTS IN 1930

Fewer drugs and larger groups of students for each drug characterized the work of 1930.

In view of the somewhat favorable showing of sulphur in 1929, it was tried again in 1930, sulphurous acid in glycerin being the compound employed. Partly because of the low percentage of favorable results, but largely because of the large number of patients showing local irritation (13 per cent), its use was abandoned.

Thymol in hydrous wool fat and petrolatum was satisfactory in only a small percentage (17.6) of cases. However, our results indicated that it increases the effectiveness of Whitfield's ointment.

Whitfield's ointment was satisfactory in 51.3 per cent of the group in which it was used.

Iodine gave exactly the same percentage of favorable results (51.3) as did Whitfield's ointment.

Summary of Therapeutic Results

Treatment	Recovery		Two Degrees or More of Improvement		Total Satisfactory Results		Worse		No Improvement		Less Than 2 Degrees of Improvement		Irritation		Worse Due to Irritation		Total Irritation		Total Unsatisfactory Results		Total	
	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent
Whitfield's ointment	11	22.9	12	25.0	23	47.9	1	2.1	10	20.8	13	27.0	0	00.0	1	2.1	1	2.1	25	52.0	48	99.9
Whitfield's ointment, plus 1.5% thymol	9	29.0	11	35.4	20	64.4	0	0.0	1	3.2	10	32.2	1	3.2	1	3.2	2	6.4	11	35.4	31	99.8
Sulphurous acid with glycerin	11	25.5	4	9.3	15	34.8	2	4.6	8	18.6	13	41.8	4	9.3	1	2.3	5	11.6	28	65.0	43	99.8
Iodine with glycerin	18	31.7	14	24.6	32	56.3	2	3.5	3	5.3	18	31.7	1	1.8	0	0.0	1	1.8	25	44.0	57	100.3

Summary.—With sufficiently large groups of students to make our figures seem worth while, we investigated the results of therapy with sulphur, thymol, Whitfield's ointment and iodine. Our results indicated that Whitfield's ointment and iodine were of the most value.

STUDIES OF THERAPEUTIC RESULTS IN 1931

During 1931, we tried a pine oil, a chlorine solution, ultraviolet rays from the cold quartz lamp, Whitfield's ointment plus thymol and a complex iodine compound.

The pine oil, with 39.7 per cent of satisfactory results, might seem worthy of further trial, but it did not measure up in effectiveness to iodine or to the compounds with Whitfield's ointment. The same statement holds true for the chlorine compound which contained 4.5 per cent of sodium hypochlorite in water. We studied the use of chlorine solutions in foot baths as a prophylactic measure in our gymnasium. The results of the study will be reported later.

Because of various claims in regard to the efficiency of ultraviolet rays from the cold quartz lamp, they were given an especially favorable trial. A special applicator was made for us. This applicator consisted of projections which could be fitted between the toes of the patients. The treatment was given several times a week. Only 17.6 per cent of the patients showed satisfactory improvement.

Whitfield's ointment, plus 1.5 per cent thymol, made a good showing, with 60 per cent of satisfactory results.

Having been impressed with the favorable showing of iodine as judged by its action on spore suspensions and on scales taken from the skin, we desired to give it further trial. Hoping to favor deep penetration, Dr. Groll of the Shell Development Company synthetized an iodine compound for us. This was chemically *di*-iodo-*di*-ethyl-sulphide and was essentially mustard gas with the chlorine replaced by iodine. Although we obtained some favorable responses to this compound, a local irritation developed from it in too high a percentage of patients to warrant further trial. We believe that further similar experiments leading to the perfection of penetrating vehicles for iodine are in order.

COMMENT

A summary of the more interesting compounds tried in the three years is shown in the accompanying table. The old stand-by, Whitfield's ointment, gives a good showing, with 47.9 per cent of satisfactory results. But it should be especially noted that when 1.4 per cent thymol is added to it, the satisfactory results jump, appreciably, to 64.4 per cent. It should also be carefully noted that the percentage of patients showing irritation under treatment with this combination is fairly high (6.4). The remedy should therefore be used with considerable caution.

Sulphur does not create so favorable an impression.

Iodine would seem to be of considerable interest in view of the high percentage of satisfactory results (56.3), as well as the highest percentage of cures (31.7) and the low percentage of irritation (1.8). It should be remembered that iodine possesses fungicidal activities in extremely high dilutions (from 1:100,000 to 1:250,000), and that it was the most effective drug that we tried while working with spore suspensions and infected cutaneous scales. We are especially hopeful in regard to iodine; we are at present trying it in the form of foot baths and ointments in a much larger series of cases.

RECURRENCE OF INFECTION OF THE FEET DUE TO RINGWORM FUNGUS

ALBERT STRICKLER, M.D.
AND
WILLIAM H. McKEEVER, M.D.
PHILADELPHIA

The problem of recurrence in epidermophytosis involves two main factors: reinfection from outside sources and renewed activity by fungi previously implanted within the epiderm.

Prophylaxis against reinfection from outside sources has received the attention of such observers as Osbourne, Gould, Samuel Ayers, Jr., and Henderson. In their investigations, they proposed various applications and methods for the prevention of this form of reinfection, such as disinfection with formaldehyde and immersion of the feet in solutions of sodium hypochlorite and sodium thiosulphate.

Reinfection through the renewed activity of the dormant ringworm organisms in the epidermis has not been given much serious consideration, for the only contribution on this subject in the American dermatologic literature is the recent publication of Jamieson and McCrea. As a result of their histologic studies of skin infected by ringworm they concluded: (1) that invasion of the skin by ringworm mycelia may be either superficial or deep (in their series, nine cases showed deep involvement of five or more layers; fourteen, superficial); (2) that the severity of the disease is directly proportional to the depth of the tissue invasion; (3) that of the eight reported recurrences, seven belonged to the superficial group; (4) that in many instances in which the onset was severe and acute, the recovery was rapid and recurrences have not been reported, and (5) that the depth of the involvement and the type of the fungus have no relationship to recurrences.

Our interest in this problem was to ascertain, if possible, the reason for the appearance of new lesions of ringworm on the normal skin in the vicinity of previously existing infections. The thought occurred that the ringworm fungus may extend beyond the limits of the lesions, invade the apparently normal tissues, remain dormant and unmolested and await favorable conditions to produce definite cutaneous lesions. It was therefore decided to examine the normal skin adjacent to active lesions for a distance of from 1 to 2 inches (0.5 to 0.9 cm.) and

From the Research Dermatologic Clinic, the Skin and Cancer Hospital of Philadelphia, Albert Strickler, M.D., medical director.

determine whether the elements of the ringworm fungus might be present. This series consisted of eighteen cases of epidermophytosis, of which nine were of the intertriginous type, six of the vesicular, two of the circinate and one of combined intertriginous and vesicular type. The plantar surfaces were affected in six instances, the interspaces in eight and both regions in four. On microscopic examination, the active lesions showed mycelia in seventeen of the cases studied; spores were found in only one instance. The normal skin on the plantar and dorsal surfaces was scraped in all directions in each of the eighteen subjects studied, and whereas the usual distance from the active lesion was 1 inch (0.5 cm.) in some instances, the normal skin at a distance of 2 inches (6.9 cm.) was examined. In six instances, mycelia were found in the normal epiderm; in four, only spores; in two, both mycelia and spores, and in six, normal findings. In the intertriginous variety, fungi were found in the normal epiderm in six instances; whereas normal findings were recorded in four; in the vesicular type, there were five instances in which mycelin were found and one in which they were not; in the circinate type, mycelia were present in one case and absent in one case. In three instances fungi were found on the dorsal surfaces; in two, on the plantar and dorsal surfaces, and in thirteen, on only the plantar surfaces. Epidermophytid lesions of the hand were found in only five patients; of these, three showed vesicular lesions, one a lichenoid, papular eruption, and one a circinate lesion.

These observations seem to indicate that in a certain percentage of patients suffering from epidermophytosis, especially of the vesicular type, ringworm fungi are to be found for some distance (for from 1 to 2 inches [0.5 to 0.9 cm.]) in the normal epiderm beyond the borders of the active lesions. In these situations the fungi await favorable opportunities to produce new lesions. This seems a fruitful method adopted by the ringworm fungus not only to prolong the individual attack but also to insure an opportunity for reinfection. Our data agree with the observations of Jamieson and McCrea, since in their study they found that in eight cases of reinfection, seven were of the superficial type; this indicates that reinfection is favored by the ability of the fungus to extend under the surface rather than by its ability to penetrate.

It therefore seems that in the treatment of epidermophytosis it is essential to apply the remedies to the apparently normal skin adjacent to the lesions as well as to the active lesions. By this procedure it may be possible to render the adjacent epiderm an unhappy habitat for the outspreading fungus. We are still somewhat in doubt as to the best technic to be used in the treatment of the widespread types of epidermophytosis. At present we are copying nature's method in its combat against the invasion by ringworm fungus, as illustrated in the clinical picture

of tinea circinata in which the most intense resistance to the advancing foe is offered at the border of the lesions. We therefore apply the most intense treatment to the epiderm about the lesions apparently unaffected by the disease, so as to render this locality unfavorable soil for the habitat and growth of ringworm infection. The epidermis already affected by the somewhat devitalized fungus disease is, in this scheme of treatment, subjected to less intense measures. The treatment employed is the vacuum vaporized iodine method.

It is our intention in the near future to publish our results with this method of treating epidermophytosis.

802-808 Pine Street.

IODIZED TABLE SALT AS AN ETIOLOGIC FACTOR IN IODODERMA

PAUL E. BECHET, M.D.
NEW YORK

The use of salt as a flavoring agent for food dates from early antiquity. The founder of Buddhism, Arddhia Chiddi, a native of Capila near Nepaul, mentioned it in his "verbal instructions." Moses, in the Book of Job, written in 1520 B. C., asked: "Can anything which is unsavory be eaten without salt?" As Moses was brought up in the court of Pharaoh, he may have derived his knowledge of the use of salt from the early Egyptians. The ancient Jews obtained their supply of salt from the Dead Sea. With the progress of civilization and the refinement of the culinary arts, salt became more and more of a kitchen necessity.

Iodine, discovered by Courtois of France in 1812, was first combined with table salt by M. Grange of Geneva, Switzerland, and used in the treatment of goiter as early as 1840. The use of iodized salt in this country dates from 1924, when it received the endorsement of the Committee of the Pediatric Section of the Michigan State Medical Society as a prophylactic measure in the prevention of goiter. It was first manufactured by the Salt Producers Association on May 1, 1924, and soon marketed throughout Michigan. In the treatment and prevention of simple goiter, iodized salt has received the enthusiastic endorsement of many eminent authorities. Hartsock[1] quoted the following from an address made by Dr. Charles H. Mayo before the Wayne County Medical Association on Jan. 26, 1924: "Iodine is almost an absolute preventive of goiter. That has been proved beyond question. Given in table salt it is a preventive for goiter." Slemmons,[2] the city health commissioner at Grand Rapids, Mich., stated: "Iodine is not a medicine. It is simply a replacement of one of the needed elements in food. We urgently ask that the people of our city use iodized salt both for the table and in cooking."

The Council of Pharmacy and Chemistry[3] of the American Medical Association decided that iodized salt could be used on the initiative of

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Read at the Fifty-Sixth Annual Meeting of the American Dermatological Association, Inc., Chicago, June 8, 1933.

1. Hartsock, C. L.: Iodized Salt in Prevention of Goiter: Is it a Safe Measure for General Use? J. A. M. A. **86**:1334 (May 1) 1926.

2. Slemmons, C. S.: Hygeia **4**:3 (Feb.) 1926.

3. Annual Meeting of the Council on Pharmacy and Chemistry, J. A. M. A. **98**:1375 (April 16) 1932.

the public, as it was suitable for public use. The question of a "safe percentage of iodine" was to be passed on in a future investigation. *Hygeia* during 1925 to 1926 carried many full page advertisements of the Morton Salt Company advocating the indiscriminate use of its iodized salt, which contained 0.02 per cent of iodine in each 2 pound package. Despite these eminent medical endorsements, Plummer [4] stated that there was a rapid increase in the incidence of exophthalmic goiter and adenomatous goiter with hyperthyroidism in 1924. This increase reached its height in 1926 and 1927, and did not diminish until 1931. The endorsement of iodized salt in the treatment and prevention of goiter has not been unanimous, and the literature pro and con has been voluminous.

THE FREQUENT USE OF IODIZED SALT

Kimball [5] stated that the Wholesale Grocers Association did all they could to bring about its exclusive sale. The same author stated that by 1926 a survey revealed that 91 per cent of the homes in Michigan were using iodized salt continuously and exclusively. In a letter to Roy D. McClure, chief surgeon of the Henry Ford Hospital, under date of Sept. 1, 1931, the largest salt distributor in Michigan stated that in 1930 he had shipped 58,643 cases of iodized salt and 7,057 cases of plain table salt. Letters from other chief distributing salt companies corresponded with these figures. This enormous consumption of iodized salt is probably limited to the sections of the United States in which goiter is endemic; yet in New York City, which is not in the goiter belt, I have personally ascertained that one large chain grocery store company with approximately 100 retail branches, sells 2,000 packages of iodized salt a month, The largest retail grocery house in the city sells in its single store 144 packages a month. On inquiring in a few grocery stores, I was told that iodized salt was occasionally sold, even when it was not requested.

AMOUNT OF IODINE IN IODIZED SALT

The amount of iodine in iodized salt does not coincide with the amount declared on the label. This has been conclusively proved by Geagley,[6] in 1929, by the analysis of 19 specimens selected in the open market; of the 19 there was a marked deficiency in all but 1. The accompanying table prepared by Geagley is of interest. Of the 19 specimens, 9 contained potassium iodide and 10 sodium iodide. It will be seen that 0.02 per cent is the amount claimed on the label by the large majority

4. Plummer, H. S.: Collected Papers of the Mayo Clinic, Philadelphia, W. B. Saunders Company, 1931, vol. 23, p. 545.

5. Kimball, O. P.: Efficiency and Safety of Prevention of Goiter, J. A. M. A. **91**:454 (Aug. 18) 1928.

6. Geagley, W. C.: Iodized Salt, Am. J. Pub. Health **19**:991 (Sept.) 1929.

of salt manufacturers. By 1932, according to McClure,[7] the iodized salt in Michigan contained 0.01 per cent sodium iodide. The salt producers estimated that each person in Michigan consumed from 5 to 6 pounds (2.2 to 2.7 Kg.) per year. Other estimates placed it as high as 8 pounds (3.6 Kg.) per year. The Advisory Committee of the Pediatric Section of the Michigan State Medical Society approved of the latter figure as most probably correct; this gave about 7 mg. of sodium iodide per person per week. This was considered well within the safe limit and efficient in the prevention and treatment of simple goiter.

Iodine Content in Iodized Salt (Geagley)

Iodine Claimed, per Cent	Iodine Found, per Cent	Excess Deficiency, per Cent
0.02	0.002	—0.018
0.02	0.019	—0.001
0.02	0.02	.....
0.02	0.007	—0.013
0.02	0.005	—0.015
0.02	0.014	—0.006
0.02	0.017	—0.003
0.02	0.0026	—0.0174
0.02	0.019	—0.001
0.02	0.01	—0.01
0.02	0.0153	—0.0047
0.02	0.0152	—0.0048
0.02	0.018	—0.002
0.02	0.018	—0.002
0.02	0.021	0.001
0.023	0.018	—0.005
0.02	0.0133	—0.0067
0.023	0.016	—0.007
0.02	0.0184	—0.0016

DANGERS FROM INGESTION OF IODINE

Death from iodine saturation or allergic sensitivity to this drug is not as rare as one would commonly suppose. Pusey,[8] at the Thirty-Fourth Annual Meeting of the American Dermatological Association in 1911, presented the photograph of a baby who died within a week from an iododerma, caused by the ingestion of iodine in its mother's milk. Iodine was found in the child's urine.

Tiefenbruner[9] reported the death of a woman, aged 49, following the taking of 12 teaspoonful doses of a solution of potassium iodide containing 5 grains (0.324 Gm.) to a dose. The lesions were of the fungating tuberous variety.

7. McClure, R. D.: Iodized Table Salt and Goiter Surgery in Detroit, Wisconsin M. J. **31**:519 (Aug.) 1932.

8. Pusey, W. A.: J. Cutan. Dis. **29**:309 (May) 1911.

9. Tiefenbruner, Georg: Ueber einen Fall von Ioderma tuberosum, Dermat. Ztschr. **29**:206 (April) 1920.

Danel [10] observed a fatal vegetating iododerma in a man, aged 51, who had taken 50 cg. of iodine daily for three or four days. Neumann [11] observed a death from medication with potassium iodide for only six days. Iodine was present in the urine. The eruption consisted of large, ulcerated tuberous lesions. Postmortem examination demonstrated similar lesions on the gastric mucosa. Eller and Fox [12] reported a fatal case of the fungating tuberous type in a man, aged 31, after the ingestion of 15 grains (0.972 Gm.) of potassium iodide daily for four months. This patient had been taking iodized salt on his food for several years. Shelmire [13] reported seven cases of severe, inveterate acne in women. All seven patients had used iodized salt exclusively for a period of from six weeks to one year. To none had iodides been administered medicinally. Irradiation and routine treatment for acne proved useless. All recovered on the cessation of the use of iodized salt. Shelmire expressed the belief that a patient with an inveterate acne, past the age when acne usually develops, should be questioned as to the use of iodized salt. The same author is of the opinion that iodized salt is not a harmless agent, and that in view of the fact that doses as small as 3 grains (0.194 Gm.) of the iodides have caused alarming symptoms, iodized salt should not be used indiscriminately. In none of his seven cases was the salt prescribed by a physician.

Goeckerman [14] observed several cases of iododerma without the history of ingestion of the drug. It does not seem improbable that these patients might have been taking iodized salt, and that this fact might have escaped his notice.

Malignant types of iododerma, variously termed "iodide sarcoma," "iododerma tuberosum fungoides" and "anthracoid iododerma" have been reported by Besnier,[15] Pospielov,[16] Hallopeau,[17] Hutchinson,[18]

10. Danel, M. L.: A Fatal Case of Bullous and Vegetating Iododerma, Bull. Soc. franç. de dermat. et syph. **33**:40, 1926.

11. Neumann, J.: A Peculiar Type of Eruption of the Skin and of the Gastric Mucosa Due to Iodine, Arch. f. Dermat. u. Syph. **48**:323, 1899.

12. Eller, J. J., and Fox, E. C.: Fatal Iododerma, Arch. Dermat. & Syph. **24**:745 (Nov.) 1931.

13. Shelmire, Bedford: Acne from Iodized Salt, J. A. M. A. **90**:1869 (June 9) 1928.

14. Goeckerman, W. H.: Iododerma and Bromoderma, Minnesota Med. **12**:408 (July) 1929.

15. Besnier, E.: Un cas d'éruption bulleuse due à l'Iodure de potassium, Ann. de dermat. et syph. **3**:168 (March 25) 1882.

16. Pospielov: A Case of Iododerma Tuberosum Fungoides, Russk. J. Kozhn. i Ven. Boliezn. **25**:200 (March) 1913.

17. Hallopeau, H.: Vegetating and Atrophic Form of Pemphigus Referable to Iodine, Ann. de dermat. et syph. **9**:286, 1888.

18. Hutchinson, J.: Iodide Sarcomata, Brit. J. Dermat. **19**:441, 1907.

Walker,[19] Fordyce,[20] Rosenthal,[21] Hyde [22] and others. In almost every instance in which the dosage could be ascertained, the eruption began after the administration of small amounts of iodides, in some cases, much less than the usual medicinal dose.

REPORT OF CASES

CASE 1.—*History.*—J. V., an Italian, aged 45, was admitted to the Stuyvesant Square Hospital on Dec. 10, 1931. He stated that he used iodized table salt both in his food and at the table for several months. About a month previous to his admission he consulted his family physician for a "rash" on his body. He was told by this physician that his blood was "doubtful," and he was given 10 drops of a solution of sodium iodide three times a day. He stated that he did not take more than 60 drops of this solution in all, so that he could not have taken more than a total of from 40 to 50 grains (2.6 to 3.2 Gm.) of sodium iodide, yet within a few days the eruption had enormously increased.

Physical Examination.—The entire surface of the skin, including the face, was covered with bright red, indurated papules and many bullae. The patient's temperature was 103 F., and he seemed prostrated.

Course.—With the passing of time, the eruption underwent a complete metamorphosis. The papules and bullae enlarged and increased in number. Central necrosis appeared, and in many of the lesions on the trunk, deep gangrenous areas developed. Some of these areas became aggregated, with consequent enlargement of the gangrenous plaques. As the sloughs separated, a superficial ulceration supervened. With the advent of the gangrenous areas, the patient's general condition became greatly aggravated. The temperature chart presented the typical step-ladder rise in the evening observed in deep sepsis. The patient was drowsy, and seemed so dangerously ill that his death was expected momentarily. The eruption showed no signs of improvement until January 27, when there was a decided change for the better. The improvement then became rapid. By February 6, no new lesions had appeared, and the patient was discharged after complete retrogression of the lesions had taken place. It was many months before he was well enough to return to work. He was last seen on Dec. 12, 1932, and at that time he seemed entirely well.

Laboratory Examinations.—The urine was normal except for traces of albumin and several granular casts. Determinations of iodide in the urine showed the following: December 17, 1.467 Gm. per liter; December 21, 1.73 Gm. per liter; December 26, negative, and Jan. 3, 1932, negative. Determination of bromide in the urine gave negative results.

The blood counts showed from 12,000 to 16,000 white cells; otherwise they were normal. The blood chemistry was as follows: Sugar, 99 mg. per hundred cubic centimeters; uric acid, 4.95 mg., and chlorides, 433.5 mg. The Wassermann,

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19. Walker, Norman: Ioderma, or Dermatitis Tuberosa Due to Ingestion of Iodide of Potassium, Lancet **1**:571 (March 12) 1892.

20. Fordyce, J. A.: Notes on Drug Eruptions, J. Cutan. Dis. **13**:496 (Dec.) 1895.

21. Rosenthal, O.: Ioderma Tuberosum Fungoides, Arch. f. Dermat. u. Syph. **57**:3, 1901.

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Kline and Kahn tests were negative. The blood cultures on three occasions were negative. The Widal reaction was negative. The culture was negative for Bacillus paratyphosus A and B. The Bacillus melitensis group showed agglutination with typhoid antigen in dilutions of 1:40 but not in those of 1:80. The agglutination tests were negative with paratyphoid A and B.

The sputum was negative for tubercle bacilli. Streptococci, pneumococci and some small unidentified bacilli were found. There were a few pus cells scattered through the field.

The feces were negative for Bacillus typhosus, but a heavy growth of Bacillus pyocyaneus was present.

Section from a fresh lesion showed an inflammatory reaction in the corium. In some places the epidermis had entirely disappeared except for a few layers of cells. The inflammatory exudate consisted of swollen connective tissue cells and some lymphocytes. There was a marked amount of edema in the epidermis.

Section from an old lesion showed a normal epidermis. There was dense round cell infiltration, including polymorphonuclear cells in the upper layer of the corium. A moderate amount of pigment was present. Culture from a bleb showed many staphylococci.

CASE 2.—*History.*—A. R., aged 24, stated that he had always used much salt on his food, and about one year previously had taken iodized salt for two months. On Aug. 21, 1932, he felt a heaviness in his chest and in one day took about an ounce of a cough mixture, of which the ingredients were unknown. One week later a generalized eruption appeared. At the time he also took, on the advice of his physician, a colloidal iodine preparation in doses of a teaspoonful three times a day for two days, whereupon the eruption became greatly aggravated. The eruption had persisted and even increased in extent for three months, at which time the patient came to the dispensary for relief.

Physical Examination.—The patient's entire body was covered with large somewhat indurated dark red papules; even the face was involved. His temperature was normal, and his general health unaffected. He was well nourished, weighing 146 pounds (66.2 Kg.). He was admitted to the hospital for observation.

Course.—The patient remained in the hospital for two months. The eruption slowly subsided during his stay, and when he was discharged had almost disappeared. The treatment which seemed most active in causing the disappearance of the eruption consisted mostly of 150 cc. of physiologic solution of sodium chloride intravenously, at first daily, then three times a week.

Laboratory Examination.—Four separate urinalyses gave negative results, as did the special examination for bromine. Two separate tests for iodine early in the treatment revealed: 0.052 mg. in 1,000 cc. of urine and 0.1 mg. in 1,890 cc. of urine. Four subsequent analyses for iodine, after several weeks of treatment, were negative. The blood counts were normal. On November 1 the Kline, Wassermann and Kahn tests were negative.

The epidermis was fairly normal. There was a slight infiltration about the blood vessels, which were slightly thickened but on the whole not engorged. The cellular infiltration was lymphocytic.

SUMMARY

1. It has been shown that iodized salt has been recommended indiscriminately to the public, which has been assured of its safety, despite the fact that severe iododermas and even death have followed the

administration of iodine in less than medicinal doses. Five deaths after comparatively small doses of the iodides are cited from the literature.

2. Seven cases of severe, inveterate acne from the ingestion of iodized salt alone are again presented for attention.

3. Two cases, one of which was nearly fatal, are reported in which the severe iododerma occurred after exceedingly small doses—case 1, 50 drops of a solution of sodium iodide, probably a saturated one; and case 2, 6 teaspoonfuls of a colloidal iodine preparation in two days, after the ingestion of iodized salt. This at least suggests that the ingestion of iodized salt sensitizes the patient to such an extent that less than medicinal doses of the iodides may cause severe iododermas, with even death as a possibility.

4. It is not my intention to condemn the use of iodized salt, as it has proved of great value in goitrous districts, but it is my duty to call attention to its dangers as either a direct cause or at least a sensitizing agent in the occasional development of severe iododermas, which, though rare, are nevertheless to be watched for. Certainly, the use of iodized salt for years without medical supervision is, from a dermatologic standpoint, fraught with a certain danger.

ABSTRACT OF DISCUSSION

Dr. Robert C. Jamieson, Detroit: In the goiter belt, as we are, and encountering so many patients who use iodized salt as a routine measure, we are finding increasingly often that many patients have their symptoms unrelieved by ordinary measures. This is particularly true in cases of acne, as Dr. Bechet mentioned. I think we should be grateful to him for bringing out the fact that iodized salt is detrimental to many patients. Patients from the age of 35 years up have very persistent acne, of acne rosacea type, with hard, quite red papular lesions. This is found so frequently that I make it a rule to have these patients discontinue the use of iodized salt before attempting medication, and often the condition clears up without medication. This was emphasized in an English woman seen about a year ago who had never suffered from acne. Within a month after she came to this country, acne of a severe type developed. With no history of a previous acne, I thought it might be iodism and had her discontinue iodized salt. Following this and the use of saline solution intravenously, she made a prompt recovery.

I think the paper of Dr. Bechet should call the attention of dermatologists, particularly in the goiter belt in Michigan and Canada, to the fact that various cutaneous lesions may be more promptly cured by stopping the use of iodized salt as a routine measure.

Dr. Jeffrey C. Michael, Houston, Texas: I wish to mention a case of chronic urticaria due to iodized salt. This case occurred in a wife of an army officer, and she discovered the cause of the trouble herself. She has had great difficulty in keeping herself free of urticaria because she has certain social duties which she must perform and it is sometimes impossible to avoid this salt entirely, but by the use of ordinary table salt she remains free from urticaria. If she gets even a small amount of iodized salt she has a recurrence of the eruption.

Dr. Sigmund Pollitzer, New York: These cases bring to mind the fatal case reported by Dr. Eller two years ago, which was interpreted by some as mycosis fungoides. It was a clear case of bullous iododerma due to a few therapeutic doses of potassium iodide in a man who had been using iodized salt for several years and evidently had become sensitized. There was considerable criticism of the paper at that time, and it was said that iodized salt could not do that; that iodides were too soluble and diffusible to be retained in the system. But, as a matter of fact, the patient excreted iodides in his urine for the three months of his stay in a hospital, during which special care was taken to exclude iodine from his diet, and at necropsy a few square centimeters of his skin yielded a considerable amount of salt.

Dr. Bedford Shelmire, Dallas, Texas: When I published my paper some years ago on the causation of iododermas from the use of iodized table salt, no proof was presented to confirm the theory that the small quantities of iodine ingested in this salt caused the specific eruptions. Two of the patients presented were later induced to ingest this substance again. In both instances there was a return of the iododerma. As the eruptions disappeared when iodized salt was removed from the diet and recurred when this condiment was again ingested, it was proved that a person sensitive to iodine can present an eruption from the small quantities of iodine contained in a salt thus medicated.

Dr. James H. Mitchell, Chicago: I have seen a number of these cases, the most definite one being that of a man, aged 35, who had had acne during the adolescent period. He had been married for two years and was much disappointed because he had been under the impression that marriage was good for acne, but he was now married, and the acne was worse than ever. His wife was a great believer in iodized salt. He had never heard of it, but went home and found they had been using it for two years. Its use was stopped; his acne has cleared up, and he has had no trouble for several months.

INHIBITION OF FUNGI IN CULTURES BY BLOOD SERUM FROM PATIENTS WITH "PHYTID" ERUPTIONS

SAMUEL AYRES, JR., M.D.
AND
NELSON PAUL ANDERSON, M.D.
LOS ANGELES

The contribution of Williams [1] in suggesting the probable allergic nature of erythematosquamous and vesicular lesions of the hands or "phytids" in association with fungus infections of the feet has opened up entirely new methods of approach to many hitherto obscure and intractable eruptions. Based on the original observations of Jadassohn [2] and Bloch,[3] who described secondary allergic reactions to deep fungus infections, Williams' conception of a similar process in the superficial fungus infections has received ample confirmation by Wise, Sulzberger, Peck, W. Jadassohn and others.[4]

These secondary phytids have been likened to tuberculids that result from some primary focus of infection. Recent trends of opinion regard these lesions as manifestations of an allergic or hypersensitive state of the tissues. Since fungi are usually easily demonstrated in the original areas of infection, which most commonly occur on the feet, and are usually absent in the secondary lesions, which are most frequently on the hands, and since some investigators [5] have on rare occasions demon-

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Read at the Fifty-Sixth Annual Meeting of the American Dermatological Association, Chicago, June 8, 1933.

1. Williams, C. M.: Diagnosis of Some Eruptions on Hands and Feet, Arch. Dermat. & Syph. **5**:161 (Feb.) 1922; Dermatophytid Complicating Dermatophytosis of Glabrous Skin, ibid. **13**:661 (May) 1926.

2. Jadassohn, J.: Ueber die Trichophytien, Berl. klin. Wchnschr. **55**:489, 1918.

3. Bloch, B.: Les trichophytides, Ann. de dermat. et syph. **2**:1 (Jan.) 1921.

4. (*a*) Sulzberger, M. B., and Wise, Fred: Ringworm and Trichophytin: Newer Developments, Including Practical and Theoretical Considerations, J. A. M. A. **99**:1759 (Nov. 19) 1932. (*b*) Sulzberger, M. B., and Kerr, Phyllis: Trichophytin Hypersensitiveness of Urticarial Type, with Circulating Antibodies and Passive Transference, J. Allergy **2**:11 (Nov.) 1930. (*c*) Jadassohn, W., and Peck, S. M.: Epidermophytide der Hände, Arch. f. Dermat. u. Syph. **158**:16, 1929. (*d*) Peck, S. M.: Epidermophytosis of the Feet and Epidermophytids of the Hands, Arch. Dermat. & Syph. **22**:40 (July) 1930.

5. Peck.[4d] Strickler, Albert; Ozellers, Edward A., and Zalatel, Ralph P.: Modern Interpretation of Mycotic Infections of the Feet and Hands: (Three Positive Blood Cultures in 290 Cases Cultured, All Three in Cases with "Phytid" Eruptions), Arch. Dermat. & Syph. **25**:1028 (June) 1932. Sulzberger, M. B.: The Pathogenesis of Trichophytids: The Spontaneous Passage of Formed Elements (Spores) From the Primary Lesion into the Circulating Blood, ibid. **18**:891 (Dec.) 1928.

strated fungi in the blood stream of patients with that type of infection and in experimental infections in animals, it is assumed that the phytid eruptions are caused by the combination of the destruction of fungi which have entered the blood stream and an altered reactivity of the tissues, usually of the hands but occasionally of other parts of the body.

This implies the simultaneous development of immunity and allergy. The relationship between these two phenomena is a matter of argument. Some investigators regard them as two phases of a single process, always occurring together, although certain recent experiments with animals tend to show that they are distinct and can be easily separated. Rich,[6] for instance, has demonstrated that pneumococci injected intradermally into immunized and desensitized rabbits are immobilized and agglutinated at the site of injection in the absence of any allergic reaction and with scarcely any evidence of inflammation.

Furthermore, it is a matter of common observation that immunity to infections such as diphtheria, smallpox and measles occurs without the development of allergic manifestations on superficial contact with the causative agents of these diseases. The organisms on coming in contact with the throat, tonsils, skin and other areas of such immune persons are apparently killed without any resulting explosive allergic reaction. This may be said to represent true immunity. On the other hand, disorders such as chronic arthritis and lupus erythematosus, regarded as manifestations of bacterial allergy, may continue indefinitely without the slightest evidence of disappearance of the causative bacteria in the tonsils, nasal sinuses or other foci of infection.

It is possible that these instances of so-called bacterial allergy—and we might include fungus allergy or phytid eruptions—represent a partial immunity which is associated with a hypersensitivity of the tissues. In other words, there are insufficient antibodies in the epidermis (of the feet in epidermophytosis; of the tonsillar crypts in certain streptococcic infections) to prevent the growth and multiplication of the parasites. Such antibodies apparently must be present in the case of the diseases which confer a permanent immunity. The blood stream, however, is capable of developing antibodies which promptly kill any invading organisms with a resulting toxic or allergic reaction manifesting itself in various ways according to the nature of the infection. Thus the allergic reaction is a response of the tissue to the toxic substance of the bacteria or fungi killed by the antibodies in the blood. If the blood did not contain such antibodies, the host would rapidly die of septicemia.

On the other hand, the effects of this protective mechanism may be annoying; in fact, they usually produce much more disability than the

6. Rich, A. R.: The Mechanism Responsible for the Prevention of Spread of Bacteria in the Immune Body, Bull. Johns Hopkins Hosp. **52**:203 (March) 1933.

original infection. Attempts have been made to alter the reactivity of the skin by a series of small desensitizing injections of the fungus proteins. Apparently no one has attempted to develop an epidermal immunity which would prevent the establishment of a fungus infection. The fact that such an antifungus immunity exists naturally in the scalp of adults, whether or not it is due to specific antibodies, should at least furnish a rational basis for further investigation along this line.

The immediate purpose of this report, however, is to record the fact that fungicidal antibodies occur in the blood in superficial fungus infections which are accompanied by allergic or phytid eruptions. That such eruptions are manifestations of hypersensitiveness to fungus proteins has been suggested by numerous reports of positive reactions to intradermal injections and contact applications of fungus proteins in the form of trichophytin.

It is not clear that these phytid eruptions represent a true manifestation of allergy in the sense that the more commonly understood use of of the term implies. No one has made any systematic attempt to study these cases of so-called fungus allergy in relation to the usual conception of the word. Allergic persons apparently inherit a constitutional predisposition to become sensitized to various antigens: foods, pollens, molds, epidermal proteins, etc. Such persons usually exhibit their allergic tendencies from infancy or childhood throughout life in varying forms, such as eczema, urticaria, asthma, hay fever, migraine and gastrointestinal symptoms. Phytid eruptions undoubtedly represent an altered reactivity of the skin, and they would furnish excellent material for a statistical study as to whether this phenomenon is related to the symptom complex described.

Previous writers on the subject of phytid eruptions have placed most of their emphasis on the allergic or hypersensitive tissue phase of the problem. We feel that the altered reactivity of the tissues is entirely secondary to and dependent on the development of a hematogenous immunity of which circulating fungicidal antibodies are at least one important expression. Per and Braude[7] indirectly mentioned the occurrence of fungicidal antibodies in allergic patients (presumably referring to persons showing phytid eruptions) by stating that parasitic fungi ceased growing within two days after being mixed in vitro with blood serum of allergic subjects. They stated further that "the serum of patients with trichophytosis treated with trichophytin does not exhibit any inhibiting influence on the parasites." The principle of growth-inhibiting antibodies against bacteria has been used for a number of

7. Per, M., and Braude, R.: Diagnostic and Therapeutic Value of Trichophytin in Dermatomycosis in the Light of Present Knowledge of Specific Allergy and Immunity, Acta dermat.-venerol. **9**:1, 1928.

years by Solis-Cohen [8] and others in the preparation of specific vaccines. In preparing vaccines from feces, sputum, etc., Solis-Cohen has made a practice of testing each bacterial strain against the patient's blood. Bacteria whose growth was inhibited by the patient's blood were considered to have stimulated sufficient immunity and were discarded, while only those bacteria which grew luxuriantly in the patient's blood and were therefore regarded as virulent were utilized in making the vaccine. Jessner [9] has also described growth-inhibiting antibodies in the blood serum of patients hypersensitive to fungi.

Numerous investigators have lamented the fact that no reliable test was available which was capable of differentiating phytid eruptions of the hands from those caused by various internal or external agents. No claim is made that such a test has been developed, but the interesting behavior of fungi when inoculated on culture mediums containing blood serum from such persons arouses the hope that some practical application may be found for the phenomenon.

THE FUNGUS GROWTH-INHIBITING PHENOMENON

As we were unaware of the work of Jessner, Solis-Cohen or Per and Braude, the idea for this experiment was probably born of the statement attributed to several sources, namely, that phytid eruptions were in all probability caused by a hypersensitivity of the tissues resulting from the destruction of fungi which had entered the blood stream. If the fungi were destroyed by the blood, the blood must contain circulating fungicidal antibodies. The technic of the test is simple.

Scales and vesicles from various areas on the hands and feet were examined microscopically in 40 per cent potassium hydroxide. Material was also cultured separately from the hands and feet on Sabouraud's medium.[10] From 5 to 10 cc.

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8. Solis-Cohen, Myer: Some Causes of Failure of Specific Vaccine Treatment and Their Correction, M. J. & Rec. **125**:727 (June 1) 1927.

9. Jessner, Max, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1928, vol. 11, p. 361.

10. The formula for Sabouraud's medium used in the experiments consisted of: maltose, 40 Gm.; peptone, 10 Gm.; agar (shredded), 20 Gm., and tap water, 1,000 cc. The ingredients were added to the water and placed in a cotton-stoppered flask, which was then placed in a cold autoclave. The pressure was allowed to rise slowly until it had reached 15 pounds' pressure. The autoclave was shut off and allowed to cool slightly. The flask was then removed, and the medium was filtered through a thin layer of cotton and gauze, tubed, stoppered and sterilized at 15 pounds' pressure for thirty minutes. On removal from the autoclave the tubes were slanted and allowed to cool in that position. The medium was left at room temperature for three days to check the sterility and then placed in the refrigerator for future use. The medium was not titrated. Neither acid nor alkali was added, as Sabouraud claims that this destroys some of the nutritive value of the medium for the growth of fungi.

of blood was withdrawn and allowed to clot. The serum was separated and mixed in the proportion of 8 per cent with a tube of Sabouraud's medium which had been heated just enough to cause the agar to melt, and allowed to cool again almost to the point of congealing. The serum was thus not subjected to heat. This serum agar must be kept in the refrigerator until ready for inoculation, since the inhibiting antibodies are destroyed by exposure to room temperature.

Fig. 1.—Inhibition of fungus growth (middle tube) shown by 8 per cent serum taken from patient with "phytid" eruption of the hands and definitely proved epidermophyton infection of the feet. The epidermophyton isolated from the patient's feet was used in this experiment. The tube on the left containing 8 per cent normal serum reveals no inhibition of fungus growth. Likewise the control tube on the right shows no inhibition of growth.

In the great majority of cases the cultures from the hands remained sterile, while fungi grew on those from the feet. As soon as a growth

was well developed, a transplant was made onto ordinary Sabouraud's medium as a control and onto another tube of Sabouraud's medium containing 8 per cent of the patient's serum. In practically all cases showing phytid eruptions the fungi were completely inhibited on the serum agar, whereas they grew luxuriantly in the control tubes and in tubes containing serum from normal persons and from persons with

Fig. 2.—Photomicrograph of a degenerated mycelium. This was found on microscopic examination of the culture mediums in tubes which showed complete inhibition of fungus growth with the addition of 8 per cent serum of the patient.

epidermophytosis without secondary phytids. If no growth occurred in either of the original cultures, it was our custom to test stock cultures of several of the more common fungi against the patient's serum.

OBSERVATIONS

Over a period of two years fifty-six cases of epidermophytosis, including four normal controls, have been studied by means of the

inhibition test. A statistical summary is recorded in the table. Particular attention is called to the fact that in eighteen cases of epidermophytosis with phytid eruptions in which various types of epidermophyton were isolated, complete inhibition took place in seventeen cases, and partial inhibition, in one. This is in striking contrast to the results obtained in the other four groups, including epidermophytosis without phytids, simultaneous infections of the hands and feet, epidermophytosis with atypical eruptions elsewhere and normal controls. In a combined total of twenty-one cases, complete inhibition occurred in only two cases;

Summary of Observations on Fifty-Six Cases of Epidermophytosis

Type of Case	Epidermophyton on Culture				Other Organisms Cultured, Including Pleomorphic Forms of Epidermophyton				Negative Culture (Test with Stock Culture)				Total			
	Positive	Negative	Delayed	Total Number of Cases	Positive	Negative	Delayed	Total Number of Cases	Positive	Negative	Delayed	Total Number of Cases	Positive	Negative	Delayed	Total Number of Cases
Epidermophytosis with phytids	17	0	1	18	1	8	0	9	4	5	0	9	20	12	1	35
Epidermophytosis without phytids	1*	4†	0	5	..	..	..	..	0	1	0	1	1	5	0	6
Simultaneous infection of hands and feet	0	3	3	5‡	0	2	0	2‡	..	..	..	..	0	5	3	5‡
Epidermophytosis with atypical eruptions elsewhere	0	4	0	4	..	..	..	..	0	2	0	2	0	6	0	6
Normal controls	..	..	..	..	..	..	..	..	0	4	0	4	0	4	0	4

* This patient had phytids one year before, although at the time this test was made the eruption was limited to the feet. Two years before, she was free from infection, and her serum failed to inhibit a culture of E. interdigitale which was inhibited by the serum of a patient with phytids.

† In one of these cases, a second specimen of serum tested sixteen days after the first gave a positive inhibition test. The patient was not seen again, so it is not known whether phytids developed or not.

‡ Two or more types of fungi were found in one case.

one of these patients had a typical phytid eruption a year previously, and the other, a recent infection of the feet without phytids which gave a negative reaction at first, although blood taken on her last visit, sixteen days later, gave a positive reaction. We were unable to determine whether phytids developed following this last test. On the other hand, of the combined group of twenty-one cases, twenty showed negative reactions, and three, partial inhibition. In some of these twenty-one cases, tests were made for more than one organism; this accounts for the apparent discrepancy of addition.

COMMENT

This series of cases is relatively small, and we fully realize that the number of control subjects, i. e., normal persons and the patients with cleancut primary fungus infections without phytid eruptions, is inade-

quate. However, for some reason, possibly owing to current economic conditions, few patients with infections limited to the feet have been observed. It is only when the lesions appear on exposed areas such as the hands that they seek medical advice.

The selection of 8 per cent serum for the experiments was purely accidental. This happened to be the amount available in the first case, and it was apparently adequate. In one case four concentrations of serum were tested, 8, 6, 4 and 2 per cent. The fungi were completely inhibited by the first two, but grew readily on the 4 and 2 per cent serums.

In some cases of clinically typical epidermophytosis with phytids no culture could be obtained from the feet, even though microscopic examination of scrapings revealed fungi. The serum of these patients was tested against stock cultures.

Several possible explanations might be offered to account for the failure of inhibition of Monilia, Cryptococcus, pleomorphic forms of Epidermophyton and Staphylococcus aureus in cases in which these organisms were isolated. In the first place, there is evidence to show that all of these forms are unusually resistant. In experiments on fumigation which we recently carried out it was found that practically double the concentration of fumes of formaldehyde was required to kill cultures of Monilia and Cryptococcus as compared with several types of epidermophyton. Pleomorphism is also regarded by some as an adaptation to adverse conditions of growth. The strain of Staph. aureus which was obtained from a typical case of dermatitis repens of the hand with "bacterids" of the hands and feet was resistant to bacteriophage and was therefore also of a resistant type. Another possible explanation for the failure of inhibition, of course, would be that the organisms in question were coincidental saprophytes and unrelated to the eruption.

A few instances were noted in which inhibition of growth was not complete but in which the patient's serum definitely retarded the growth of the fungus as compared with the control by as much as ten days. This usually occurred in patients in whom fungi were found on both the feet and the hands, and it probably represents only a partial development of fungicidal antibodies.

We have not as yet determined the duration of immunity of the blood in patients with phytid eruptions. One patient who had a typical transitory eruption of phytids about a year ago, and who now shows lesions confined to the feet from which fungi were cultivated, gave a positive reaction to the inhibition test, showing that antibodies are still present. Theoretically, if organisms from the feet were to gain entrance to the

blood stream, an eruption of phytids would again develop. Incidentally, this prompt destruction of fungi on entering the blood stream probably accounts for the rarity of positive blood cultures.

As the result of observations extending over a period of about two years we have come to regard this procedure as of some value in determining the nature of certain atypical eruptions. The test is by no means infallible, but it furnishes one more bit of evidence which in obscure cases may act as a guide in the matter of treatment. When a patient's blood serum inhibits the growth of a fungus obtained from the feet, we have usually been correct in assuming an accompanying eruption on the hands to be a phytid. We have felt even more certain, however, that an eczematous eruption of the hands or other parts of the body is not related to a fungus infection of the feet if the inhibition test is negative for the patient's own organisms if they belong to the Epidermophyton group.

CONCLUSIONS

Circulating fungicidal antibodies have been demonstrated in the serum of patients having phytid lesions associated with epidermophytosis. The presence of the antibodies was proved by failure of growth of fungi isolated from the primary focus of infection and inoculated on Sabouraud's medium mixed with 8 per cent of the patient's serum.

As a result of observations on fifty-six cases the following conclusions may be drawn: 1. Fungi cultured on Sabouraud's medium containing 8 per cent serum from a normal person show no inhibition of growth.

2. Epidermophytosis without phytids usually shows no inhibition.

3. Simultaneous infections of the feet and the hands show no inhibition or partial inhibition.

4. Epidermophytosis of the feet and phytids of the hands usually show complete inhibition of growth except when Monilia, Cryptococcus or pleomorphic Epidermophyton is the causative organism.

5. Epidermophytosis of the feet and unrelated eczema of the hands show no inhibition.

This procedure has already been of value in the differential diagnosis of some obscure eruptions of the hands.

2007 Wilshire Boulevard.

DISCUSSION

DR. HOWARD FOX, New York: This paper is of value in that it attempts to aid in differentiating vesicular eruptions of the hands, especially those associated with eruptions of the feet. The authors have used autogenous cultures mainly, and stock cultures when unable to obtain autogenous ones. I should like to know

whether their results with these two methods were equally satisfactory. Dr. Ayres spoke of using a pleomorphic culture. Pleomorphism as defined by Sabouraud refers to a degeneration which takes place in culture mediums containing sugar and not in the skin. A pleomorphic growth could be obtained from the skin only by previous inoculation of an already pleomorphic culture. The speaker said that there was complete inhibition in cases of phytids of the hands but none in cases of "nonrelated eczema" of the hands. The question is: How did they differentiate between phytids and eczema, which are often so similar clinically?

Dr. J. G. Hopkins, New York: This appears to be an important presentation, but it is difficult to evaluate it without observation of the actual experiments. It would be of interest to know whether Dr. Ayres tested the cultures which failed to grow to see whether they were killed or merely inhibited. Bactericidal antibodies are difficult to demonstrate, except against gram-negative bacteria, and their action is most striking against fragile forms such as the cholera vibrio. I believe that fungicidal antibodies have not been demonstrated previously. The bactericidal antibodies either kill promptly or are without effect. If a few bacteria survive the first period of exposure, they multiply in the antiserum. If Dr. Ayres' investigation has shown an inhibitory action by immune serum, I believe that it reveals a hitherto unknown type of antibody action and is of the utmost importance.

Dr. Charles M. Williams, New York: I wish to raise one point in connection with conclusion 4, which states that "Epidermophytosis of the feet and phytids of the hands usually show complete inhibition of growth except when Monilia, Cryptococcus or pleomorphic Epidermophyton is the causative organism." I take it to mean that in those cases all he found on the feet was infection caused by Monilia or Cryptococcus. That does not mean that the lesions were not phytids, because we fail to find the organism in many cases, and it is important to know in how many cases of frank phytids he found only cryptococcic infection of the feet. If the finding occurred in only 50 per cent, then his results are not quite as convincing as they would be otherwise.

Dr. Samuel Ayres, Jr., Los Angeles: I appreciate this discussion very much.

Answering Dr. Fox, I assure you that I did not conclude that merely because certain cultures were not inhibited we were, therefore, dealing with nonrelated eczemas. The eruptions in the majority of cases in this group were not at all typical of phytids. One started with lesions on the hands that one might have thought were phytids, but a generalized exfoliative dermatitis developed which lasted several months and was found to be due to arsenic. There happened to be a fungus infection of the feet, but I do not believe that the two processes were related.

Some of the pleomorphic organisms spoken of here began on original culture as typical fungi, and then within a few weeks the pleomorphic changes started to develop. Others were apparently pleomorphic from the beginning; that is, they grew all over the surface of the medium without any definite configuration and with abundant aerial hyphae. Whether this pleomorphism was due to contact with these immune antibodies I do not know.

As to whether the inhibited organisms were really killed or not, we have only recently investigated this phase of the subject, but we have found some rather interesting things. After a culture has failed to grow for two or three weeks it can be taken out of the tube and examined. Under the microscope a few degenerated organisms will be found which have become swollen and which in some

cases have taken on an appearance suggestive of the mosaic bodies occasionally seen in examinations of fresh scales or scrapings. However, these organisms will not grow, for we have inoculated fresh tubes of Sabouraud's medium with this material, and they have remained sterile.

Regarding Dr. Williams' question about Monilia and Cryptococcus, the latter was found only once. When the patient was last seen, the eruption had practically cleared up following the use of a variety of parasiticides. The lesions on the hands responded without any treatment as the infection of the feet cleared up. We have examined the lesions repeatedly and never found any organism except Cryptococcus, which was obtained twice by culture. We have found Monilia, I think, in only three cases; this is not a large enough incidence to draw conclusions from.

DR. CHARLES M. WILLIAMS, New York: I am much interested in the so-called mosaic fungus, and the photograph Dr. Ayres showed did not have the form of a mosaic at all.

RECALCITRANT PUSTULAR ERUPTIONS OF THE PALMS AND SOLES

GEORGE C. ANDREWS, M.D.

FREDERICK W. BIRKMAN, M.D.

AND

RICHARD J. KELLY, M.D.

NEW YORK

During the past five years increasing attention has been devoted to the study of dermatoses of the palms and soles which resemble ringworm infections but which are not mycotic. In 1928, Mitchell [1] reported a series of cases. The previous year Barber and Eyre,[2] Dore [3] and Roxburgh [4]—all in England—published papers dealing with similar disorders. In 1929, Lehmann [5] presented before this section several cases of pompholyx and emphasized the importance of internal disturbances in them.

Barber [6] clarified the meaning of the term acrodermatitis continua and called attention to the fact that it is the same disorder that was described as dermatitis repens by Crocker; he also described the generalized eruptions which may develop from the localized form of the disease. He has shown that these conditions are infective and are due to Staphylococcus aureus, and that this group should be regarded as chronic pyogenic dermatitis. For the sake of clarity, it is well to mention the principal clinical features of acrodermatitis continua vel perstans.

From the Department of Dermatology, Vanderbilt Clinic, College of Physicians and Surgeons, Columbia University.

Read before the Section on Dermatology and Syphilology at the Eighty-Fourth Annual Session of the American Medical Association, Milwaukee, June 14, 1933.

1. Mitchell, J. H.: Amycotic Dermatoses Simulating Ringworm and Erosio Interdigitalis Blastomycetica, Arch. Dermat. & Syph. **19**:659 (April) 1929.

2. Barber, H. W., and Eyre, J. W. H.: Acrodermatitis Continua (Hallopeau) vel Dermatitis Repens (Crocker), Brit. J. Dermat. **39**:485 (Dec.) 1927.

3. Dore, S. E.: Note on Cases of a Chronic Mild Localized Type of Acrodermatitis Perstans, Brit. J. Dermat. **40**:12 (Jan.) 1928.

4. Roxburgh, A. C.: Two Cases of Acrodermatitis Perstans, Brit. J. Dermat. **40**:27 (Jan.) 1928.

5. Lehmann, C. F.: Acute Vesicular Eruptions of the Hands and Feet, Arch. Dermat. & Syph. **21**:449 (March) 1930.

6. Barber, H. W.: Acrodermatitis Continua vel Perstans (Dermatitis Repens) and Psoriasis Pustulosa, Brit. J. Dermat. **42**:500 (Nov.) 1930.

The disease usually begins on the extremity of a digit, either as an infected traumatic sore or as paronychia. Thus at the beginning it is unilateral and localized, but from this initial site the infection may spread so as to involve other extremities, and rarely it may become generalized. Audry [7] and Barber [6] have emphasized the particular importance of the involvement of the nails, which are affected as in ordinary paronychia. The early, elementary lesions are intra-epidermal pustules, and the visible pustules at this stage are formed by the confluence of such microscopic abscesses and may be of considerable size. By rapid peripheral spreading a crusted patch is formed. Barber stressed the histologic similarity between acrodermatitis continua and Civatte's [8] hypotheses regarding psoriasis. He called attention to the fact that in both conditions there is the same tunneling of the rete by migratory leukocytes, the same "abscess-formation" with intracellular edema and the same process of parakeratotic exfoliation. The similarity in the mechanism of production of the two eruptions perhaps explains the psoriasiform appearance of some lesions of acrodermatitis.

An abortive form of acrodermatitis suppurativa continua, usually confined to the palms and soles, was described by Audry [7] in 1901. In 1930, Ingram [9] considered this abortive form a noninfective disorder, possibly a separate entity, and accepted the suggestion of MacLeod and Barber that the term pustular psoriasis is appropriate for it. The onset, course and clinical appearance of this condition contrast strikingly with those of true acrodermatitis continua, as do the bacteriologic findings.

The cases which we shall describe have a close resemblance to those called pustular psoriasis of the extremities by these authors. Indeed, Barber's description of the clinical features fits our cases so closely that we have been tempted to quote it.

CLINICAL FEATURES

We wish to report fifteen cases which have clinical features similar to the description of pustular psoriasis of the extremities, but to which we are reluctant to attach this term. The outstanding clinical features of this small group are the distribution of the eruptions, the symmetry and the recalcitrance. The distribution is so constant that it is impressive. The sites of election are (1) the midportions of the palms, from

7. Audry, C.: Les phlycténoses récidivantes des extrémités acrodermatities continués de Hallopeau, Ann. de dermat. et syph. **2**:193, 1901.

8. Civatte, A.: Psoriasis and Seborrhœic Eczema: Pathological Anatomy and Diagnostic Histology of Two Dermatoses, Brit. J. Dermat. **36**:461 (Nov.) 1924.

9. Ingram, J. T.: Acrodermatitis Perstans and Its Relation to Psoriasis, Brit. J. Dermat. **42**:489 (Nov.) 1930.

which the eruption spreads to the thenar and hypothenar eminences and eventually may cover the entire palm and the flexor surfaces of the fingers, and (2) the insteps, from which it may extend peripherally on to the heels or the balls of the feet, or may spread ultimately so that the entire plantar aspect is involved. It may also extend upward onto the lateral and mesial surfaces of the feet for a short distance. In one patient the eruption began simultaneously on both heels. There is never any involvement between the fingers or toes, or of the interdigital webs. Occasionally small groups of pustules were noted on the

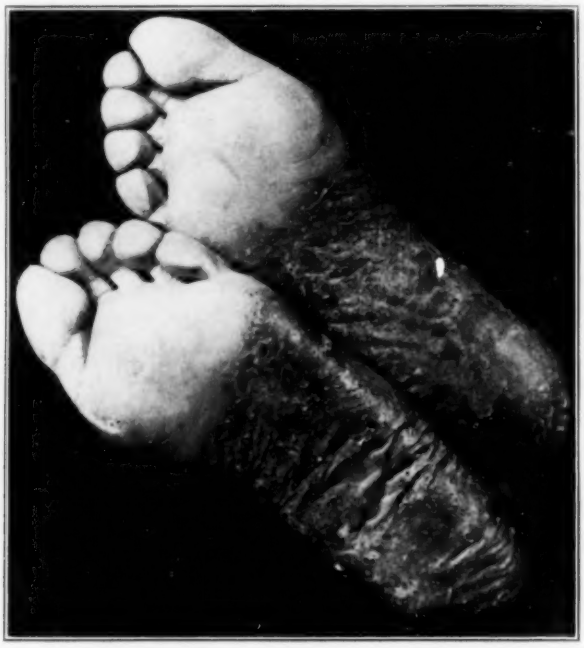

Fig. 1 (case 5).—Typical distribution on soles after one and one-half years' duration. Note the symmetry. The affected areas show innumerable small pustules in various stages of development. The toes and the anterior portion of the sole are entirely free from eruption.

tips of the toes. Instead of spreading by peripheral extension, outlying patches, separate from the original patch, may develop.

The patches themselves are well defined and vary in appearance, according to their particular stage of development. At the beginning they are either vesicular or pustular. If there are vesicles, they become seropurulent in a few hours so that the lesions are chiefly purulent. These vesicles and pustules are small and discrete, and if not opened they dry up, leaving a brown spot, which Barber spoke of as an intraepidermal scab. In the course of further development, the pustules

exfoliate, and ultimately the exfoliation becomes profuse and forms one of the cardinal features of the eruption. As a consequence, the patches may resemble the skin of patients suffering from generalized exfoliative dermatitis, except that the involvement is limited to small areas in the locations described. Generally, however, in addition there are present throughout the patch, but principally at the margins, vesicopustules, pustules and tiny brown scabs of dried up pustules. Exacerbations occur without explanation, being evidenced by intense burning of the parts and the appearance of new pustules, chiefly at the edge of the patch. After a few days, new pustules appear in decreasing numbers, and the patient becomes more comfortable. In the quiescent stage, the patch is erythematous and scaly with occasional discrete, pinhead-sized, fresh or dried up pustules. Fissuring may occur, as may excoriations, for the patches are very pruritic, and the patient is tempted to scratch and rub them or to pull off the scales.

Although the eruption has a tendency to affect both palms and soles, it frequently begins on only one palm or one sole, the opposite member becoming involved within a short time. Sometimes, however, the eruption may be limited to one extremity for a long period. Usually, it is bilateral from the very beginning, with about equal incidence on the hands and feet, and in 80 per cent of our cases the eruption spread so as to involve all four extremities.

As Barber pointed out, the absolute symmetry and the fact that the eruption may appear bilaterally *ab initio* are features that distinguish the condition from true acrodermatitis continua, which begins as a localized, unilateral, infective lesion, often of traumatic origin. This symmetry suggests that the eruption is due to a blood-borne toxin or organism and not to an external infection.

LABORATORY EXAMINATIONS

When the laboratory findings are compared, a most important distinction between this condition and acrodermatitis continua is revealed. In the latter condition the cutaneous lesions show an infection with Staphylococcus aureus, whereas in the cases of pustular psoriasis and in our group of cases the most careful microscopic and cultural examinations almost invariably gave negative results.

In practically every case repeated cultures have proved completely sterile. These cultures were made again and again from fresh pustules and from excised tissue, in blood broth and on dextrose and blood agar. Autoinoculation was invariably unsuccessful. Intradermal inoculation of guinea-pigs with emulsified tissue and with the contents of the pustules caused no local reaction, local abscess or any sickness in the animal. Likewise, when material from our patients was rubbed into the feet

of guinea-pigs, it did not cause any local disease. Gram and Giemsa staining of excised tissue have revealed no micro-organisms.

A frequent finding in our group was, however, a blood count that suggested some chronic reaction to an infective agent. We were impressed by the fact that several patients had high white cell counts, without corresponding increases in polymorphonuclear cells. The counts were suggestive of moderate neutropenia, which means either a normal or a moderately high white cell count without a corresponding increase in the number of polymorphonuclears. This was not so in all cases, but occurred with sufficient frequency to lead us to investigate further for an internal cause of the disorder.

ASSOCIATED CONDITIONS

As a result we found that most of our patients had obvious foci of infection in other parts of the body. Some had abscessed teeth, and others had grossly diseased tonsils, chronic sinus trouble, duodenal ulcer, chronic colitis or arthritis. In other words, our search has shown that all of our patients had focal infections, and a large proportion of them had severe focal infections.

Until treatment was instituted for the accompanying focal infections no permanent improvement was elicited. Our patients did not respond to roentgen therapy or to any of the remedies ordinarily used in the treatment of psoriasis, eczema or ringworm. The only cures obtained were in cases in which the focal infections were eradicated, and the only treatments which were of benefit otherwise were immunologic ones consisting of injections of autogenous vaccines, boiled milk and staphylococcus toxin. For local use, the remedy which uniformly was most beneficial was a solution of aluminum acetate, applied diluted either in the form of wet dressings (from 1:20 to 1:5) or in wool fat (1 or 2 drachms or 3.9 or 7.8 Gm. to each ounce).

All of the patients were adults. All were given repeated mycologic examinations of the feet, hands and nails and had negative trichophytin tests; some were also tested with extract of Monilia. Cultures for Monilia were made not only from the skin but also from the feces and scrapings of the tongue.

HISTOPATHOLOGY

Histologic examination revealed a fairly uniform picture. The report of Dr. Gerald F. Machacek is as follows: Parakeratosis was seen which varied considerably in amount. In some sections it was marked, and in other sections it was very slight. No stratum lucidum was distinguished. The granular layer was prominent and wide. There was a generalized edema of the stratum spinulosum. The edema caused

the intercellular bridges to stand out prominently. A moderate acanthosis was present. In general the basal cell layer was well preserved. The rete pegs were elongated; some were thin. Wide masses of epithelium also projected into the corium. A few papillae projected upward and were surmounted by papillary beds of epithelium, which were relatively narrow.

The unique pathologic feature was the formation of pustules in the epithelial layers. A few small collections of leukocytes were seen in the thick keratin layer. More striking, however, were the intra-epithelial pustules which were observed in these sections. They were either single or multiple. One specimen, instead of showing large pustules roughly covering the area of a low power field, contained vesicles, which were intra-epithelial. A few small satellite groups of swollen, clear epithelial cells contained vacuoles, and among them were seen fairly numerous polymorphonucleocytes.

The usual picture, as we indicated before, was a large intra-epithelial pustule. The roof of this pustule was the keratin layer. The sides were composed of squamous cells. The floor, also of epithelial cells, was thin and was made up of the basal layer with two or three layers of squamous cells above it. Some of the pustules showed a loss of all epithelial cells in that portion of the wall which formed the floor. In these cases the contents of the pustule were in direct contact with the corium. Coil gland ducts were seen to be in close relation to the wall of the pustule. In one instance the duct passed into the pustule. The contents of the pustule consisted not only of numerous polymorphonuclear cells but also of epithelial cells in all stages of degeneration. Part of the cytoplasm of some of the cells was basophilic. More often, however, the swollen cytoplasm, which had lost all vestige of prickles, was homogeneously eosinophilic. The nuclei were large and vesicular or small and pyknotic. Some of the degenerated epithelial cells were large and round. Other epithelial cells were irregular in shape and had retained the general outlines usually associated with stratified squamous epithelium. About the periphery of the pustule were seen a few polymorphonuclear cells, both in the epithelium and in the adjacent corium. Quite close to the pustule the polymorphonuclears were numerous but quickly diminished in number to only an occasional one a short distance from the lesion.

The corium contained very few polymorphonuclears. These were seen in considerable numbers only in those sections where the floor of the pustule was devoid of epithelium and where the contents of the pustule were in direct contact with the corium. The reaction in the corium was very slight. A fair number of lymphocytes was seen just beneath the epithelium. These were chiefly in the perivascular and

Fig. 2.—*A* (case 5), photomicrograph showing a typical intra-epithelial pustule from the sole. Note the mass of polymorphonuclears and epithelial débris in the pustule, the moderate acanthosis, the thickening of the granular layer and the very slight infiltration of the corium. *B* (case 8), photomicrograph of a section from the palm. Note that the histologic characteristics are strikingly similar to those in the section from the sole in case 5 (*A*). *C* (case 4), section from the sole, showing similar histologic features, except that the stratum corneum is extremely flaky. Clinically, the lesions were in an exfoliative stage.

perineural tissue. Edema of the corium was present. The coil glands showed no definite pathologic involvement. In the neighborhood of one of the pustules was seen a meissnerian nerve ending, which seemed to have undergone degeneration and was eosinophilic.

Sections stained by Gram's method showed no organisms. Giemsa stain disclosed no bacteria or fungi but showed a few mast cells in the infiltrate of the corium.

More accurately stated, the sections represented a pustular intraepithelial lesion which was striking because of the slight reaction in the surrounding epithelium and adjacent corium.

REPRESENTATIVE CASES

The following cases have been selected to illustrate the principal points that have been made.

CASE 1.—In Mrs. R. R., aged 33, a patient of Dr. J. Gardner Hopkins, the eruption began in October, 1931, simultaneously on the palms and soles. There had been frequent recurrences since the onset. There were no lesions on the sides or webs of the digits. Mycologic examinations gave negative results, and cultures showed no growth. At about the time of onset the patient had a severe sore throat and previously had had occasional attacks of tonsillitis. She had been advised by an otolaryngologist to have her tonsils removed.

The lesions consisted of minute, deep vesicles and pustules, some with a hemorrhagic zone about them. They appeared in groups on the palms and soles, associated with desquamation, but there was no diffuse inflammation. The individual lesions seemed smaller and deeper and suppurated more promptly than the lesions of trichophytosis.

Various treatments were given with more or less benefit, but a few pustules usually persisted on the feet, and there were occasional severe relapses. In June, 1932, the tonsils were removed by Dr. George V. Browne. Two days later there was a severe outbreak of the condition on both hands and feet, but within two weeks all the lesions had entirely disappeared, and the patient was free from the disease until she had a sore throat on December 10, followed by a persistent cold, at which time there were three or four new vesicles and pustules on one foot, which promptly cleared after the cold subsided. There has been no further recurrence.

CASE 2.—In Mr. B., aged 40, a patient of Dr. Paul Gross, the eruption began in May, 1931, on the hands and feet, with the appearance of vesicles and pustules. He was treated for ringworm, without improvement. Direct and cultural examination for fungi gave negative results. Cultures for other micro-organisms were sterile. The tonsils were enlarged and diseased. The basal metabolic rate was —16. The Wassermann test was negative. A blood count showed: hemoglobin, 100 per cent; erythrocytes, 4,140,000; leukocytes, 9,500; polymorphonuclears, 61 per cent; small lymphocytes, 32 per cent; mononuclears, 3 per cent, and eosinophils, 4 per cent.

In September, 1931, as the tonsils were removed, the eruption improved. At times the patient continued to have outbreaks. He never, however, experienced any severe eruption of the skin after the tonsils were removed. A chronically

inflamed appendix was removed in August, 1932. Since that date the patient has been entirely free from cutaneous trouble.

CASE 3.—In March, 1929, the condition occurred in Mrs. G., aged 47, on both thenar eminences, and spread to the soles three months later. There were large patches of vesicles and pustules with desquamation on both insteps. The patient had been treated by many physicians. She gave no history of other diseases of the skin. Repeated examinations for fungi gave negative results. Cultures were sterile, except one for Staphylococcus albus. The eruption was constantly present and was under treatment by us for three years, during which period all kinds of remedies were tried without benefit. For months at a time the patient had wet dressings on her feet and complained of weakness and fatigue. It was recognized for a long time that her tonsils were badly diseased, but she refused to be operated on. Eventually she consented and the tonsils were removed by Dr. Morley T. Smith, who rendered the following report: "There was a fairly large adherent tonsil mass in each fossa. The tonsils showed marked infection. Culture from the tonsils showed Staphylococcus aureus and a long and short chain nonhemolytic streptococcus. A mouse inoculated with this culture died in thirty-six hours." A vaccine prepared from the culture was given. Following the operation and vaccine therapy the condition of the skin gradually subsided and finally completely disappeared. There has been a decided improvement in her general health. Now, the first time in four years, the patient is free from this eruption.

CASE 4.—In Mr. W., aged 47, the eruption began on each palm almost simultaneously about September, 1929, and two months later appeared on the soles, chiefly on the insteps. Some of the lesions were vesicles, but they rapidly became pustules, the latter becoming predominant. The pustules spread gradually from the center of the palms to the thenar eminences, and from the insteps to the soles until gradually the entire midportions of the soles were involved. Also, the eruption extended on to the sides of the feet for a short distance. As the patches spread there was a dull erythema with exfoliation, which was limited to the involved areas. There were periodic exacerbations with active pustule formation, followed by remissions.

Cultures and mycologic examinations gave completely negative results. A blood count showed 15,400 white cells. A differential count (average, 200 cells) showed: polymorphonuclears, 69.5 per cent; lymphocytes, 25 per cent; large mononuclears, 1.5 per cent; eosinophils, 3 per cent; basophils, 0.5 per cent, and transitionals, 0.5 per cent. Inoculation of material from the pustules into a guinea-pig gave negative results.

After treatment for eight months with all kinds of remedies the condition eventually subsided as a result of injections of boiled milk given in large doses (10 cc.). The patient had a recurrence about six months later and was treated by other physicians. He finally came back to us through the courtesy of Dr. Joseph W. Gardam, and having learned from experience with other cases, we searched for focal infections. He had six diseased teeth, severe pyorrhea and infected tonsils. Three weeks after the diseased teeth were extracted the eruption completely cleared, and he has had no further trouble.

COMMENT

Although some of the histologic features are consistent with psoriasis, the inconstancy of the parakeratosis, the increased granular layer in many sections and the large pustules with strikingly little reaction

about them are not ordinarily seen in psoriasis. We think that it will be admitted that the histologic changes are not sufficiently characteristic to make psoriasis a positive diagnosis without more corroborative evidence than is present in this group. The theory that the process in these sections might be a special type of psoriasis with differences depending largely on the degree of leukocytic infiltration of the dermis and epidermis is interesting.

However, there were no clinical signs of psoriasis in any of our cases; that is, there were no lesions on the skin or nails of any of our patients that we would have called psoriasis if the eruptions on the palms and soles had not been present. Thirteen of our patients had never had any other cutaneous trouble, except the eruptions on the palms and soles, and careful examination revealed that they were completely free from any other diseases of the skin. In five of the thirteen patients there was an abnormal thickening of one or more of the nails, but there was never anything in the condition of the nail sufficiently characteristic to warrant the diagnosis of psoriasis, except in case 10, in which there was stippling of one finger-nail. In two of our patients there occurred other lesions that were not incompatible with psoriasis. In one, follicular, pustular lesions developed on the extensor surfaces of the elbows and three small erythematous, scaling patches on the scalp. In the other, follicular, pustular lesions developed on one elbow and folliculitis on the sides of the thighs. In both, these eruptions lasted less than two weeks and subsided rapidly under roentgen therapy. As stated before, these eruptions might have been psoriasis, their character being indeterminate. They occurred on areas commonly affected by psoriasis and were not inconsistent with such a diagnosis. In all of the other thirteen cases, however, there was not the slightest history or suggestion of psoriasis, except for the lesions on the palms and soles and for the occasional changes in the nails, which might have been trophic.

Dyshidrosis, pompholyx and cheiropompholyx are comprehensive and vague terms which might be applied to these cases. However, the absence of hyperhidrosis, the onset in many cases during cold weather and the persistence throughout the winter, the absence of lesions on the sides of the fingers or toes, the involvement of circumscribed symmetrical areas and the chronicity and lack of response to any form of local treatment, particularly roentgen therapy, are not in accordance with the usual conceptions of pompholyx.

Whether the condition we have described is an entity in itself or an expression of some form of another disease is largely of academic importance. However, a practical feature in the report is that some patients of this group have been cured by the removal of focal infections.

SUMMARY

1. We have made a study of fifteen patients with recalcitrant pustular eruptions of the palms and soles. Our cases seem to be similar to those described by Barber and his co-workers and termed pustular psoriasis of the extremities.

2. In all cases bacteriologic and mycotic examinations failed to reveal a local causative organism.

3. These patients were extremely unresponsive to all forms of local treatment, including roentgen therapy.

4. In almost every case there were evident foci of infection. The patients whose foci of infection were removed were cured or showed marked improvement.

5. The difference between these cases and simple dyshidrosis is pointed out.

6. Among our patients none had typical lesions of psoriasis which could be definitely diagnosed as such.

7. A study of serial sections in six of our cases failed to show several important changes which are usually held essential for the histologic diagnosis of psoriasis. They did reveal, however, a fairly definite pathologic picture which would suggest that this condition is an entity.

8. None of our patients responded to therapeutic procedures which are generally effective in producing at least temporary improvement of psoriasis.

9. There is a recalcitrant pustular condition of the palms and soles, sometimes caused by focal infections, which resembles pustular psoriasis of the extremities but should not be classified as this disease.

ABSTRACT OF DISCUSSION

DR. JAMES HERBERT MITCHELL, Chicago: The subject of palmar and plantar pustules is so complex that I do not feel at all competent to discuss it. In the early days, before ringworm was commonly known, all vesication on the palms and soles was considered as dyshidrosis. Later all vesication was considered as mycotic. In 1928, in an effort to offset this impression, I reported a series of cases, some of which resembled those of Dr. Andrews. However, the response to therapy in my cases was relatively good. As to focal infection, I cannot say much for I have had little experience. One patient had carbuncles, and I have had other patients with associated staphylococcic infections. In those cases I succeeded in obtaining staphylococci from the pustules.

As regards the diagnosis of dermatitis repens, I am inclined to think in the terms of the test for witches in the old days in Salem. They were thrown into the mill pond, and if they drowned they were innocent. If a case of dermatitis repens clears up it is not in my opinion dermatitis repens. No patient with dermatitis repens whom I have treated has recovered. One patient was under the

observation of Dr. Ormsby and myself for many years, but failed to improve under any treatment. Dr. Andrews had no evidence of psoriasis elsewhere in his cases. In Dr. Ebert's series there were psoriatic lesions elsewhere as well as abundant lesions on the palms and soles. In a patient I recently demonstrated before the Chicago Dermatological Society there was an association between psoriasis and a dermatitis herpetiformis-like syndrome. The patient had these lesions on the extremities, and there was eosinophilia of the vesicle content and of the blood. The lesions responded readily to roentgen therapy. The patient can be kept free as a rule by the giving of inorganic arsenic.

Dr. George Miller MacKee, New York: Dr. Andrews and his collaborators have made a creditable and perhaps successful attempt to lessen the etiologic and nosologic uncertainties relative to pustular eruptions of the palms and soles. My discussion will be limited to psoriasis pustulosa, described by Barber. Of course, not all pustular eruptions of these parts are psoriasis. The various pyodermias attack the palms and soles, but they can hardly be confused with psoriasis pustulosa, which is not a true pyodermia. It is most often mistaken for dermatophytosis or dermatophytide. The essential difference is that the elementary lesion in the latter is a vesicle at the start, while in the former it is a pustule.

Psoriasis pustulosa is thought to be uncommon. It is usually limited to the palms and soles, but may attack other parts. There may or may not be psoriasis on other parts of the body. The nails may or may not be involved. There is likely to be an associated, unrelated interdigital dermatophytosis. The pustules are usually sterile. The disease is characterized by remissions and exacerbations. In addition to the pustules, there is usually a squamous eruption throughout the affected area. The disease is unusually stubborn and does not, as a rule, respond favorably to, or does it tolerate well, the therapeutic measures ordinarily successful in psoriasis.

Nonspecific protein therapy, protein shock, the removal of foci of infection and other constitutional measures have been employed successfully for the treatment of fixed psoriatic patches, and they may be equally useful or more so for psoriasis pustulosa.

The pathologic histology is not typical of psoriasis, but when material is obtained from a squamous area, especially between exacerbations, the microscopic picture resembles psoriasis more than any other condition. Judging from Dr. Andrews' description of his clinical material and especially judging from the photographs thrown on the screen, I believe that many, if not most, of his cases represent psoriasis pustulosa.

Dr. Marion B. Sulzberger, New York: If it could not be proved that pyogenic micro-organisms produce eruptions of this type, we should still have to assume that such eruptions must exist. The conception of staphylids is simply an enlargement of the principle of trichophytosis and trichophytids and is in accord with the theory of focal infections. In one case, there are the fungus infection beneath the toe-nails and the trichophytid on the hands. In another case, there is the focus of monilia infection in the nails, or the intestines, mouth or elsewhere, with the monilid on the hands. Since we know that staphylococci and streptococci are present in as many or more foci than fungi, and that these organisms can sensitize the skin, we must postulate the existence of their corresponding "ids." Still, we have a long way to go before we can prove a given case to be a "staphylid." We have, as yet, none of the evidence already built up by more than thirty years of research in the case of trichophytids—no cutaneous reactions (as to trichophytin), focal flare-ups,

demonstration of circulating organisms, experimental reproductions of the disease in animals and man or a therapeutic effect with specific desensitizations.

One must be careful not to argue that if an allergic condition clears up after an operation, that operation has removed the cause. We all have seen or known of innumerable cases of ragweed hay fever, of horse asthma and of fur dye dermatitis in which the condition cleared up after operation. Pasteur Vallery-Radot recently reported more than thirty cases of asthma due to known allergins in which the patients were free from attacks during periods of from months to years following various fortuitous intercurrent operations, including laparotomies under general and local anesthesia. These facts make it difficult to say now which of Dr. Andrews' cases were cases of staphylids.

Dr. Theodore Cornbleet, Chicago: I had an opportunity to study a case of pustular psoriasis in Dr. Senear's service and can corroborate some of Dr. Andrews' results. Auto-inoculation of material from a pustule gave negative results. Culture of this material on Sabouraud's medium twice grew a fungus which I was not able to classify accurately, but it belonged to the fungi imperfecti. Emulsions of this organism, when inoculated into the patient and into animals, produced no lesions. Pus inoculated into animals directly from the patient's lesions was without any positive results. I feel much as do the previous speakers, that the pustules in pustular psoriasis are simply enlargements of the microscopic ones normally found. I believe, too, as Dr. Sulzberger does, that we have to be careful in estimating results following operations such as tonsillectomies. There are so many things that affect the skin indirectly that we have to be careful in deciding whether a certain procedure affects the focus of infection or is the direct cause of the cutaneous lesions that are being observed.

Dr. Walter J. Highman, New York: The first question to arise in our minds as we heard Dr. Andrews' excellent paper was whether he was dealing with pustular psoriasis. We are not dealing with pustular psoriasis in his series because the lesions were restricted to definite areas of the body, and in no instance was there other evidence of psoriasis. Thus it seems safe to assume that we are dealing with some other type of eruption. Various conditions suggest themselves, namely, that this is one of the phytids, dermatitis repens or acrodermatitis, or a condition sui generis, which I think is what Dr. Andrews has in mind. If it is the last condition, is it due to focal infection? The fact that histologic study throws little light on the question is very easy to corroborate. Are these eruptions due to focal infections, and where are the foci? Dr. Andrews failed to demonstrate the presence of fungi. It may be because no fungi were present, or it may be that he did not select the correct material in which to demonstrate the fungi. We may therefore follow Dr. Andrews to his conclusion that these lesions were due to some cause operating somewhere in the body, and we are where we were fifteen years ago, when it was warmly debated whether or not focal infections had any bearing on disorders of the skin. I am not convinced that the rôle of focal infection in dermatoses has been demonstrated. Nevertheless Dr. Andrews' logic seems complete.

If we assume that we are dealing with an effect that is due to a cause believed to have been ascertained, it is necessary that when the alleged cause is removed the effect disappears and does not return. We need not wait seventy years for observation, but should conclude working in less than three or four. In some instances Dr. Andrews said that the eruption improved after removal of the focal infections, and in two or three instances I think he said there were recurrences. To the extent that he fails to show that the focus was actually removed, his conclusions will fail.

DR. SAMUEL AYRES, JR., Los Angeles: Dr. Highman is expecting too much of Dr. Andrews in asking him to eradicate completely all foci of infection. I have been much interested in focal infection, having been a victim myself. Removal of infected tonsils does not remove the entire source of infection. Infected tonsils frequently are secondary to sinus infections, and the latter cannot be entirely removed. Infection frequently involves the gallbladder, appendix and other organs. It is therefore not fair to state that because tonsils and teeth were removed and the eruption did not entirely clear up, this indicates that foci of infection were not the cause. The improvement in the eruptions following removal of foci is very impressive. I should like to ask Dr. Andrews whether gold preparations have been used, in view of their marked efficacy in cases of lupus erythematosus, a condition regarded as being due to a focus of infection.

DR. C. FERD LEHMANN, San Antonio, Texas: The only resemblance to psoriasis in this eruption is its chronicity and failure to respond to the ordinary therapy used in these cases. We should take into consideration the influence of local agents as well as constitutional agents. For instance, in a series of cases similar to those Dr. Andrews described, both from the local and the constitutional point of view, I found that the majority of them were cases in which there was hyperhidrosis, the skin being easily macerated. We have to take into consideration the physical influence incident to the use of the hands as a factor causing the localization of these psoriasiform lesions. The fact that there is this type of dermatitis with vesicles of the palms and soles means that we have to take into consideration that hyperhidrosis has a large part in the disorder. The fact that improvement has occurred in some cases, and cure in other cases, indicates that constitutional factors do influence the disorder.

How can we prove whether we have one or more entities? The fact that improvement of the system as a whole influences the result indicates the problem. We have no laboratory criteria to guide us; therefore, following the plan of Dr. Andrews will lead us somewhere.

DR. M. F. ENGMAN, JR., St. Louis: Dr. Andrews finds that there is something more in the eruptions of the hands and feet than ringworm. We have our own difficulty at home, in the form of pompholyx, and my father and I have seen many cases in which we had been unable to demonstrate fungi at any time. We see these cases over a period of years, sometimes with deep vesicles and pustules over the palms and soles, but we are unable to control the disease with the usual tropical applications. Roentgen therapy is fairly successful, but the lesions recur. However, we are able to control them with diet, eliminating entirely all animal food. We have no explanation of why the removal of animal foods from the diet affects these cases. For convenience, we call these phytids, but what they are we do not know.

DR. SAMUEL M. PECK, New York: Dr. Andrews is to be congratulated for pointing out that there are other pustular conditions of the hands and feet besides dermatophytosis and dermatophytids. Histologically, the sections of the skin which Dr. Andrews showed bear a close resemblance to the pustular type of dermatophytids. The flattening of the epidermis around the pustules in his sections shows that we are dealing primarily with a vesicle which caused pressure on the surrounding tissues. This is important because in epidermophytids there is first spongiosis and then vesicle formation, and finally there may be pus filling the vesicles. If we are dealing with a primary pustular condition, the vesicular stage may be missing. The very fact that there is so little inflammatory reaction

in the upper layers of the cutis speaks against a primary pustular lesion. I should like to ask Dr. Andrews if any spongiosis was noted in his sections.

Dr. Fred D. Weidman, Philadelphia: I have seen only three or four of these cases and cannot speak as authoritatively as Dr. Andrews. When I first saw the lesions in the earliest stages, there were no pustules and there was no yellow cast. I think that the idea Dr. Ayres just spoke of can be disposed of as the cause of the condition.

I should like to ask Dr. Andrews whether there was a visible connection between these vesicles and the sweat ducts, i. e., whether they could be milia. Those who have studied the literature, particularly the French, and have seen some of the excellent histologic illustrations of dyshidrosis may recall what a polemic there was as to whether vesicles did or did not communicate with the sweat ducts. It is a real histologic feat to make a decision when secondary factors like pressure complicate the picture. The same problem also presents itself here, in which case the query whether there was evidence of pressure around the vesicles, or spongiosis, would be decidedly to the point. So far as I could gather from the photographs in the scientific exhibit and the lantern slides, it appeared to me that there was only a minor grade of inflammation, and even if it should develop that these vesicles are not milia, I should still be inclined to regard them as essentially non-inflammatory.

I disagree with Dr. Highman regarding the histology in psoriasis, and I believe that some information may still be gained from these sections. They point against psoriasis, and other clinical features also point against psoriasis. If milia can be excluded, and if it is agreed that the inflammatory features are not fundamental and primary, as a last resort I wish to throw out the suggestion that the condition may be simply a matter of abnormal nutrition rather than an inflammatory process. It may be avitaminosis, or at any rate dysvitaminosis, and if dermatologists are not entirely unanimous regarding the nature of this disease, the matter of avitaminosis should be pursued further.

Dr. C. Guy Lane, Boston: Until one and one-half years ago I did not feel that diet had anything to do with these cases. We have all seen recalcitrant diseases of the hands and feet, most of which give negative results on examination for bacteria and fungi. A young physician under my care, who had an eruption of this type, volunteered the information that eggs had some effect in his particular case. He had an interval of freedom following abstinence from eggs. This has been checked several times. We have used different combinations of food, and he has had three definite attacks of this peculiar pustular eruption on the hands following the ingestion of egg as an ingredient of other foods. This suggestion has been followed in two other cases in which there has not been quite as good an opportunity to follow the dietetic history, and it seems to me that there is a possibility that eggs may have something to do with the disorder in some cases at least. In another case it appears that egg is not the sole cause. In the case of a man who has kept an accurate chart as to when pustules appear on his hands, his longest period of freedom from pustules has been during abstinence from eggs in any form. He has counted anywhere from forty or fifty to a few new pustules a day, and one of the periods of exacerbation, when the pustules numbered fifty, was associated with the taking of egg in the diet.

Dr. Clark W. Finnerud, Chicago: I wish to record about a dozen cases similar to those described by Dr. Andrews, which I have seen in the last few years with Dr. Ormsby, some of which have been studied culturally and histologically as well as clinically. Our conclusion is that it is not a fungous infection

and that it differs in all stages distinctly clinically from ringworm. Histologically, and after going over the work of Barber and the other English authors carefully, we have felt that we were not dealing with a form of psoriasis; none of our cases presented lesions of psoriasis on the body elsewhere. There is too great a tendency on the part of dermatologists to consider vesicular or pustular eruptions largely limited to the palms and soles as ringworm. Such a diagnosis should never be made without demonstration of the fungi from lesions on the foot, a procedure which requires but a few minutes.

Dr. George C. Andrews, New York: In presenting this subject rather hurriedly in the fifteen minutes allowed, misunderstandings must naturally occur. I do not wish any one to believe that I do not think that there is any such thing as pustular psoriasis. I stated that our cases did not show the features of psoriasis, and that it would be as wrong to call them pustular psoriasis as to call them ringworm, as we did several years ago. There is a great tendency now to call all pustular eruptions of the hands and feet pustular psoriasis, and that is wrong. We should call them pustular psoriasis only when they are associated with lesions of psoriasis on other parts of the body or have a history, or the histologic appearance, of psoriasis.

Dr. Mitchell's case, which developed after boils, impressed me as being of infectious origin, and probably one of acrodermatitis continua.

The differences between acrodermatitis continua and dermatitis repens are not important so far as this paper is concerned. I accept the definitions of these terms as given by Barber and other investigators.

I do not believe that all pustular eruptions of the hands and feet are due to focal infections. In some of our cases there were definite focal infections accompanied by leukocytosis. The eruptions entirely cleared after the focal infections were removed. Such cases, however, represent only a very small number of these eruptions of the palms and soles. However, we should keep in mind that such cures have been obtained, even though the number of cases is small.

In answer to Dr. Peck, I wish to state that serial sections have been made but no spongiosis was found.

As to Dr. Weidman's remarks, I was glad to hear him say that the changes in the sections were not those of psoriasis. Careful study showed no constant association of the pustules with the sweat ducts. There was no parakeratosis in many of the sections, and it was sparse and inconstant in others. I cannot conceive of psoriasis without parakeratosis. There was a marked increase in the granular layer in most sections.

Some of the patients were treated with gold solutions intravenously without benefit.

In summarizing, I should like to point out particularly that not all chronic pustular eruptions of the palms and soles with sterile pustules are pustular psoriasis. The relation of some of our cases to focal infections is a less important part of the presentation.

CUTANEOUS REACTIONS WITH "PURIFIED" OIDIOMYCIN

RICHARD BAILEY, M.D.
Fellow in Dermatology and Syphilology, the Mayo Foundation, Rochester, Minn.
AND
LEON GOLDMAN, M.D.
CINCINNATI

Oidia not only produce certain well known diseases of the skin but are often found on the normal skin, as Jessner and Kleiner,[1] Staehelin, Mu and van Schouwen [2] and others have shown. It is often difficult to decide whether the species of Oidia found in a particular case is pathogenic or only saprophytic. This question is of special interest since Ravaut and his school [3] discussed levuroses and levurides, and since the investigations made by Ramel.[4]

Several methods have been used to differentiate between pathogenic and saprophytic strains of Oidia.[5] For example, Staehelin, Mu and van Schouwen analyzed the cultures themselves. Benham,[6] Hopkins and others have used agglutination as a differential criterion. There remains, among other methods, the clinical comparison of their oidiomycins.

Oidiomycin is a preparation which should be analogous to tuberculin and particularly to trichophytin. Intradermal testing of the latter preparations gives negative reactions on normal skins. Oidiomycin does not seem analogous in this respect. Ravaut demonstrated that in twenty-four hours oidiomycin (levurine) reacts in almost every case,

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Work done in the Dermatologische Klinik, University of Zurich, Switzerland.

1. Jessner, M., and Kleiner, S.: Arch. f. Dermat. u. Syph. **149**:363, 1925.

2. Staehelin, A.; Mu, J. W., and van Schouwen, M.: Arch. f. Derm. u. Syph. **165**:294, 1932.

3. Ravaut, P.: Bull. Acad. de méd., Paris **101**:680, 1929; Presse méd. **37**:372, 1929; Ravaut, P., and Rabeau, H.: ibid. **40**:1925, 1932. Hy: Thèse de Paris, 1930.

4. Ramel: Rev. méd. de la Suisse Rom. **49**:887, 1929.

5. Jadassohn, W.: Die Immunbiologie der Haut, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1932, vol. 2, p. 385.

6. Benham, R. W.: J. Infect. Dis. **49**:183, 1931.

but he regards this as a "false" reaction. He considers only the late "true" reaction, which he interprets as an indication that the patient is infected with pathogenic Oidia. He finds this particularly true in patients who also show levurides. This reaction might be described as a "flare-up," occurring as it does several days after the "false" reaction. Just why oidiomycin produces a false reaction is a question still unanswered. Several possibilities exist. Are these false reactions due to impurities masking the "true" reaction, or is it possible that in reality these are not "false," and that every person reacts to oidiomycin in a specific manner? As Oidia occurs on the skin of nearly every person, the reaction may be analogous to the positive tuberculin reactions found in nearly every adult living in thickly populated centers. If this last supposition is correct, the "true" reaction of Ravaut indicates nothing more than a particularly strong "false" reaction.

The first step in deciding between these two possibilities is an attempt to purify oidiomycin, i. e., to take away as much of the substance as is possible without destroying the active principle. Bloch, Labouchère and Schaaf [7] purified trichophytin by means of a method which removes practically all the substance except the carbohydrate fraction. This carbohydrate fraction of trichophytin was found by Bloch, Labouchère and Schaaf to be active in cutaneous reactions and by W. Jadassohn, Schaaf and Sulzberger [8] in anaphylactic reactions. Similar preparations of oidiomycin were made by Kesten, Mott and others,[9] and were found to be active in precipitation and agglutination and in anaphylactic tests. It remained necessary to examine the activity of such a preparation in reactions of the skin. This we have done.

METHOD OF PREPARATION

From 6 to 8 week old, actively growing cultures on maltose bouillon (1,000 cc. of distilled water, 10 Gm. of peptone and 40 Gm. of maltose) in a 5 liter flask were employed. These were first subcultured to determine the purity of the original culture.

Each Oidium culture was incubated with 0.5 per cent phenol for twenty-four hours. The entire contents of each large flask were then centrifugated at high speed; the supernatant fluid was poured off and saved. The centrifugated residue was ground vigorously with one-tenth the volume of nutrient fluid and with an

7. Bloch, B.; Labouchère, A., and Schaaf, F.: Arch. f. Dermat. u. Syph. **148**:413, 1925.

8. Jadassohn, W.; Schaaf, F., and Sulzberger, M. B.: Klin. Wchnschr. **110**: 857, 1932.

9. Kesten, H. D.; Cook, D. H.; Mott, E., and Jobling, J. W.: J. Exper. Med. **52**:813, 1930. Kesten, H. D., and Mott, E.: J. Exper. Med. **53**:803, 1931; J. Infect. Dis. **50**:459, 1932.

equal weight of sterile quartz sand. The mixture was frozen solid by means of carbon dioxide snow and acetone, and gradually thawed. This process was repeated three times. The mixture was then centrifugated at high speed, and the supernatant fluid was combined with the previous volume of supernatant fluid. The combined volumes of these fluids were filtered through a Chamberland filter. The filtrate (the "ordinary" oidiomycin) was concentrated to one-tenth its volume in vacuo. This concentrate was added slowly, with vigorous stirring, to ten times its volume of concentrated methyl alcohol. After the flocculent, chocolate brown precipitate had settled out completely, it was separated from the supernatant fluid by suction filtration, washed repeatedly with methyl alcohol and ether, and dried thoroughly in a desiccator over sulphuric acid. This precipitate was dissolved in from five to ten times its volume of water, in divided amounts, and centrifugated repeatedly until the supernatant fluid was of a homogeneous reddish wine color, and the mass of residue did not change appreciably. The combined volumes of supernatant fluid were added to ten times their volume of concentrated methyl alcohol, and the process was repeated. This precipitation with methyl alcohol was carried out three times. After the third precipitation, the precipitate was thoroughly washed with methyl alcohol and ether and dried in a desiccator. The product was then ready for chemical analysis and for cutaneous tests.

For clinical use a 1 per cent solution was made by dissolving the required weighed amount of powder in physiologic solution of sodium chloride, heating the solution at from 95 to 100 C. for ten minutes and adding 0.25 per cent phenol. The 0.1 per cent solution was made by diluting the 1 per cent solution with sterile physiologic solution of sodium chloride.

The results of the different protein, carbohydrate and nitrogen tests were the same as those obtained by Kesten, Cook, Mott and Jobling;[9] i. e., protein tests were negative or nearly so, and nitrogen and carbohydrate tests were strongly positive.

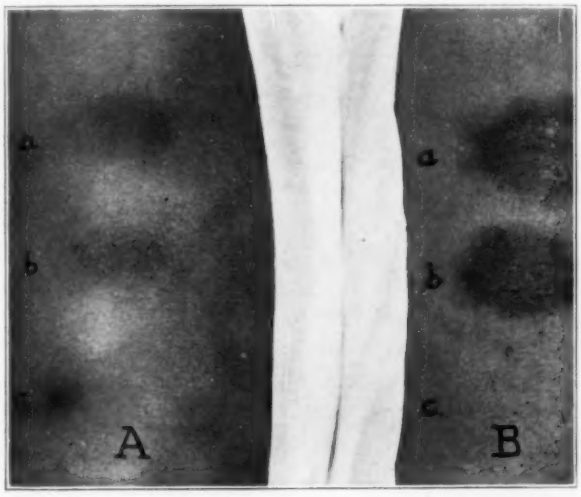
For convenience this "purified" oidiomycin, in comparison with the "trocken trichophytin" of Bloch, Labouchère and Schaaf[7] and with the "trocken tuberculin" of Bucher, Jadassohn and Schaaf,[10] was designated as "trocken oidiomycin." We made intradermal tests with a 1 per cent and a 0.1 per cent solution, in an unsefected group of twenty-eight patients, most of whom were from the wards for venereal diseases.

COMMENT

Before we speak of the results of these investigations, we must call attention to the fact that we are working with three purified oidiomycins produced from three different strains. Two were definitely pathogenic. One of these was furnished by Ravaut and the second was isolated and cultivated from the skin of a patient with the diagnosis of diabetes mellitus and oidiomycosis at the clinic in Zurich. (These same stains were used in the investigations of Staehelin, Mu and van Schouwen.) The third was isolated at the clinic in Zurich from the skin of a patient who was under treatment for gonorrhea and whose skin was apparently normal.

10. Bucher, O.; Jadassohn, W., and Schaaf, F.: Ztschr. f. Immunitätsforsch. u. exper. Therap. **76**:241, 1932.

We shall first discuss the reaction of the pathogenic purified oidiomycins, in order to compare the results with those of Ravaut who worked with "nonpurified" oidiomycins. With these pathogenic purified oidiomycins every patient gave a positive reaction from twenty-four to forty-eight hours after injection. In spite of the process of "purification," we obtained the same "false" reactions as Ravaut. We cannot decide whether these reactions are nonspecific in spite of the process of purification or whether all persons tested were hypersensitive to purified oidiomycin because of latent infections. The last assumption seems to us at least as well justified as the first.



Reactions with purified oidiomycin in a healthy child, aged 8 years, obtained with: (*a*) purified oidiomycin from the strain of Monilia, furnished by Ravaut, (*b*) purified oidiomycin from a pathogenic strain isolated from a diabetic patient, (*c*) purified iodiomycin made from strains of Monilia obtained from normal skin. *A* shows the reaction forty-eight hours and *B*, ninety-six hours after injection.

With the purified oidiomycin produced from the normal strain the reactions were negative or only slightly positive. The "slightly positive" reactions were never as marked as the weakest reactions produced by the pathogenic purified oidiomycins. This fact seems to us of certain interest. If it is possible to confirm it with purified oidiomycins made from the several other pathogenic and normal strains, it will be a step toward differentiating pathogenic from saprophytic Oidia. If this phenomenon occurs regularly, it will also confirm a sentence written by Bloch in 1928, regarding the hyphomycetic fungi: "Ganz allgemein scheint sich also (genaue systematische Untersuchungen wären aller-

dings noch sehr wünschenswert) als Regel zu ergeben, dass die Kulturen von "virulenten" Pilzen, welche in vivo hochgradig allergisierende Mykosen hervorrufen, die beste Ausbeute an Mykin liefern." [11] (Though exact systematic investigations are still much to be desired, it seems that, as a rule, cultures from virulent fungi which in living beings cause strong allergizating mycoses yield the most Mycin.)

11. Bloch, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1928, vol. 2, p. 343.

LYMPHOBLASTOMA (HODGKIN'S DISEASE) OF THE SCALP

REPORT OF A CASE

CHARLES A. GREENHOUSE, M.D.
AND
VAN ALSTYNE H. CORNELL, M.D.
NEW YORK

Hodgkin's disease was described in 1832 [1] but Sternberg [2] was the first to accurately describe the pathologic changes in this disorder. Although cutaneous manifestations of Hodgkin's disease are found, according to Ziegler,[3] in 25 per cent of all cases, according to Cole,[4] in 40 per cent, and according to Miller,[5] in 40 per cent, it was not until 1906 that Grosz [6] published a report of the first case of lymphogranulomatous [7] infiltration of the skin.

The cutaneous manifestations of Hodgkin's disease have been divided into two main groups, the nonspecific or the toxic eruptions (ides) and the specific or true lymphogranulomatous lesions.

The nonspecific or toxic eruptions are: (1) pruritus, with or without excoriations, pyodermias and lichenifications; (2) pigmentation; (3) prurigo-like eruptions; (4) bullous or pemphigoid lesions; (5) exfoliating erythrodermias; (6) purpuric lesions, scarlatiniform and morbilliform eruptions, urticaria and erythema nodosum-like eruptions, and (7) trophic disturbances, such as loss of hair and secondary changes of the nails.

Specific or true lesions appear as infiltrations, nodules, tumors or gumma-like infiltrations, in localized, disseminated or corymbose arrangement.

From the Department of Dermatology and Syphilology, New York Post-Graduate Medical School and Hospital, Columbia University, Dr. George Miller MacKee, director.

1. Hodgkin: Tr. Med.-Chir. Soc. Edinburgh **17**:68, 1832.
2. Sternberg, C.: Ztschr. f. Heilk. **19**:21, 1898.
3. Ziegler, Kurt: Berl. klin. Wchnschr. **48**:1917, 1911.
4. Cole, H. N.: The Cutaneous Manifestations of Hodgkin's Disease, J. A. M. A. **69**:341 (Aug. 4) 1917.
5. Miller, H. E.: Lymphogranulomatosis Cutis, Arch. Dermat. & Syph. **17**: 156 (Nov.) 1928.
6. Grosz, S.: Ueber eine bisher nicht beschriebene Hauterkrankung (Lymphogranulomatosis Cutis), Beitr. path. Anat. u. z. allg. Path. **39**:405, 1906.
7. Throughout this paper the terms Hodgkin's disease of the skin and lymphogranulomatous infiltration of the skin have been used synonomously.

In reviewing the literature up to 1920, Fox [8] accepted ten cases as authentic examples of lymphogranulomatous infiltration of the skin and added one of his own. In 1927, Miller,[5] in an exhaustive paper read before the fiftieth annual meeting of the American Dermatological Association, added two more cases, one from his series of fifty-five cases from the University of California Hospital and one from his private practice. Hoevelborn [9] stated that, according to Schoenhof, only fifty cases of specific lymphogranulomatous infiltration of the skin had been reported in the literature up to 1928, and that he was able to find eighteen more cases in the more recent literature.

A further subdivision of true lymphogranulomatous infiltration of the skin is the primary or initial lymphogranulomatous lesion of the skin which develops first in the skin proper; that is, it is not merely an extension from a deeper lesion or a contiguous lymph gland. It has been called by the French dermatologists *le chancre lymphogranulomateux* [10] and cases have been reported by Artz,[11] Arndt,[12] Alderson,[13] Kren,[14] Saafeld [15] Reinsberg and Kadlický [16] and Nanta and Chatellier.[10]

REPORT OF CASE

History.—W. S., a white man, aged 40, an insurance agent, born in the United States, was first seen on April 22, 1933. He complained of no symptoms except a rash on the scalp. He had three children living and well; his wife had had no miscarriages. Except for the history of a penile lesion twenty-three years before, for which he received treatment (the exact number and nature he did not remember), his family and past medical histories were irrelevant.

The patient stated that fifteen months previously he had received an injury to the scalp. Three months after the trauma, the disease began as a small pimple and gradually enlarged to the size at presentation for treatment. During the fifteen months, he had not consulted a physician or applied a medicament locally. His general health had remained unchanged.

Examination.—The patient was a well nourished man, aged 40. His pupils were equal and regular in outline and reacted promptly to light and in accommodation. His teeth revealed numerous caries. The buccal mucosa presented no abnormal manifestations. The heart and lungs were normal. The liver and spleen were not palpable. There were no enlarged lymph nodes. Examination of the bones and

8. Fox, Howard: Lymphogranulomatosis of the Skin in Hodgkin's Disease, Arch Dermat. & Syph. **2**:578 (Nov.) 1920.

9. Hoevelborn, C.: Die isolierte Lymphogranulomatose der Haut, Arch. f. Dermat. u. Syph. **166**:136 (Aug.) 1932.

10. Nanta, A., and Chatellier, L.: Ann. de dermat. et syph. **6**:682 (Nov.) 1925.

11. Arzt and Randak: Acta Dermat.-Vener. **6**:16, 1925.

12. Arndt, G.: Virchows Arch. f. path. Anat. **209**:432, 1912.

13. Alderson, H. E.: J. Cutan. Dis. **35**:481, 1917.

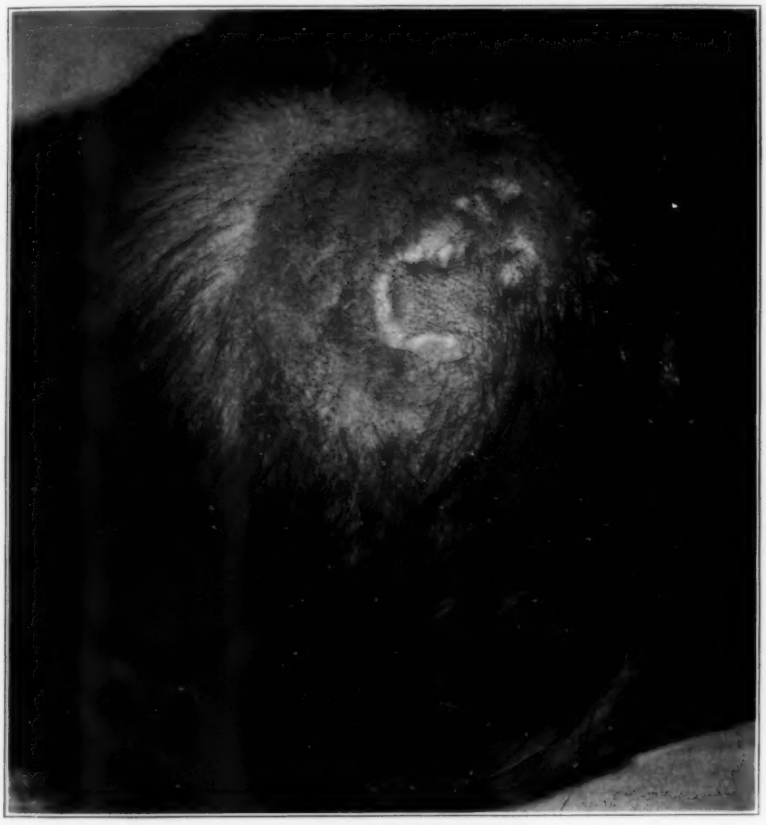
14. Kren: Arch. f. Dermat. u. Syph. **130**:549, 1921.

15. Saafeld, U.: Arch. f. Dermat. u. Syph. **148**:158, 1924.

16. Reinsberg, U., and Kadlický, R.: Acta dermat. venereol. **5**:477, 1924.

the joints revealed no pathologic changes. Neurologic examination failed to elicit organic abnormalities.

On the vertex of the scalp was an area of alopecia roughly circular in outline, measuring 7.5 cm. in diameter. About one half of the bald area (fig.) was occupied by a sharply outlined, palm-sized serpiginous, smooth, shiny, indurated lesion. It was raised about 0.5 cm. above the surface and was bluish red and slightly yellow. There was no tenderness on palpation, and it was freely movable. At the periphery of the larger lesion were several satellites, which were small, pea-



The lesion with satellites before treatment.

sized lesions of similar characteristics, but they were hidden from immediate view by the growth of hair.

Treatment and Course.—Antisyphilitic treatment was instituted, and the patient received three injections of neoarsphenamine (0.3, 0.6 and 0.6 Gm.) and five of bismuth. There was no noticeable change after four weeks, and roentgen treatment was instituted. The patient received 4 skin units of unfiltered roentgen rays (1,440 roentgens), according to MacKee's standards, over a period of six weeks. The lesions responded rapidly and completely disappeared.

Laboratory Data.—The Wassermann and Kahn tests were repeatedly negative. Chemical analysis of the blood and urine yielded normal findings. The blood

count was as follows: red cells, 4,750,000; white cells, 7,000; monocytes, 4 per cent; eosinophils, 1 per cent; bone forms, 1 per cent; polymorphonuclear leukocytes, 74 per cent; small lymphocytes, 20 per cent. Later blood counts were all about the same.

Roentgen examination of the mediastinum, chest, skull and long bones showed no evidence of disease.

Pathologic Changes.—The tissue was examined by Dr. D. L. Satenstein of the department for cutaneous diseases of the New York Post-Graduate Medical School and Hospital and Dr. P. Klemperer of the department of pathology of the Mount Sinai Hospital.

Dr. Satenstein's Report: In the midcutis and deep cutis, especially about the follicles, was a fairly compact cellular infiltration. There was moderate edema throughout the cutis. The papillary bodies were swollen. The rete pegs were poorly formed. The overlying epidermis was thinned throughout.

The vessels of the upper cutis were markedly dilated; some were empty, and some were filled with blood cells.

With the high power lens, the cellular infiltrate was found to be composed of small round cells, small and large connective tissue cells with vesicular type nuclei, some cells with a densely stained nucleus (comparatively few) and some fibroblasts. In occasional zones were groups of large cells with loose chromatin nuclei suggestive of epithelioid cells. At a few isolated spots were clumped nuclei. These may have been giant cells. In the cellular zones were some fine, thin-walled blood vessels. There were no mitoses and no degeneration of cellular elements.

The multiform character of the cells, the presence of the vessels and the possible giant cells spoke in favor of one of the granulomas.

The absence of mitoses, degeneration and pigmentation and the clumping of nuclei, together with the presence of cell nests, tended to rule out mycosis fungoides.

The absence of distinct perivascular focal cellular infiltration and normal internal and external coats of vessels ruled out syphilis.

The absence of tubercles ruled out tuberculosis.

The positive findings were suggestive of lymphogranuloma (Hodgkin's disease).

Dr. Klemperer's Report: A slide of a piece of hairy skin showed that the epidermis was moderately hornified and flattened. The superficial corium showed a slight but diffuse infiltration with inflammatory cells which were accumulated along the vessels. They were generally mononuclear cells intermingled with fewer polymorphonuclear leukocytes. Within the deeper layers of the corium there were large nodular accumulations of cells around the hair follicles. They consisted of large mononuclear cells with pale nuclei, often with conspicuous nucleoli intermingled with lymphocytes, a few plasma cells and polymorphonuclear leukocytes. Occasional giant cells with several nuclei of the type first described were found, as were fibroblasts and connective tissue fibers forming a framework within the nodules. Although the histologic picture was not absolutely characteristic, the nodular arrangement of the inflammatory cells, the type of mononuclear cells and giant cells and the pleomorphous picture of the inflammation were rather suggestive of Hodgkin's disease.

SUMMARY

Investigators in this field agree that lymphogranulomatosis cutis is one of the divergent expressions of that large group of clinical condi-

tions associated with lymphadenosis to which Mallory [17] first gave the name of lymphoblastoma. We are reporting this case because of its several unusual points of clinical interest.

1. The patient gave a clearcut history of injury to the scalp three months prior to the advent of the illness under discussion.

2. There was complete absence of subjective symptoms.

3. The lesions were located on the scalp only.

4. There were no other evidences of Hodgkin's disease discernible clinically or by laboratory tests.

5. The histologic changes were fairly typical.

6. The lesions responded rapidly to small doses of roentgen rays.

900 Grand Concourse.

40 East Sixty-First Street.

17. Mallory, F. B.: The Principles of Pathologic Histology, Philadelphia, W. B. Saunders Company, 1924, p. 326.

MONILIAL INFECTION OF THE SKIN

REPORT OF A FATAL CASE

ETHEL M. ROCKWOOD, M.D.
AND
ARTHUR M. GREENWOOD, M.D.
BOSTON

During the past few years much attention has been called to infection by Monilia. The whole subject has been admirably summed up by Hopkins,[1] and the previously confusing classification has been simplified through the work of Hopkins and Benham,[2] Stone and Garrod[3] and Stovall and Bubolz.[4]

We report here a fatal case of moniliasis of the skin. We were unable to find a similar case in the literature.

REPORT OF A CASE

History.—C. B., aged 51, married, American, a grocer, was referred to us in February, 1930, by Dr. M. M. Restall of Marblehead for a generalized eruption of the skin of one year's duration. There was no history of any previous cutaneous disease or of similar cases in his family. The disease began in the mouth, later involving the palms and then the nail folds as paronychias, the face, the neck, the axillae, the groins, the lower part of the abdomen and the upper part of the thighs. There was practically no discomfort from the eruption (except when abscesses developed). At times the mouth was sensitive, but this never seriously interfered with eating. At no time were there any gastro-intestinal symptoms, and at no time did any medication, radiation or diet have any permanent beneficial effect. The disease progressed, with much secondary infection, practically unchecked, to a fatal termination on Nov. 13, 1931.

Physical Examination.—The lesions had definite borders. They were red and dry at all times, with delicate scaling. The edges were strikingly definite. They were slightly raised but never vesicular, and for 1 mm. beyond them there was a narrow halo of erythema. The area over which the infection had

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Read before the Section on Dermatology and Syphilology at the Eighty-Fourth Annual Session of the American Medical Association, Milwaukee, June 16, 1933.

1. Hopkins, J. G.: Moniliasis and Moniliids, Arch. Dermat. & Syph. **25**:599 (April) 1932.

2. Hopkins, J. G., and Benham, R. W.: Monilia Infections of Hands and Feet, New York State J. Med. **29**:793 (July 1) 1929. Benham, R. W.: Certain Monilias Parasitic in Man; Their Identification by Morphology and by Agglutination, J. Infect. Dis. **49**:183 (Sept.) 1931.

3. Stone, Kenneth, and Garrod, L. P.: Classification of Monilias by Serological Methods, J. Path. & Bact. **34**:429 (July) 1931.

4. Stovall, W. D., and Bubolz, A. A.: Cultural and Biochemical Characteristics of Monilia Isolated from Human Sources, J. Infect. Dis. **50**:73 (Jan.) 1932.

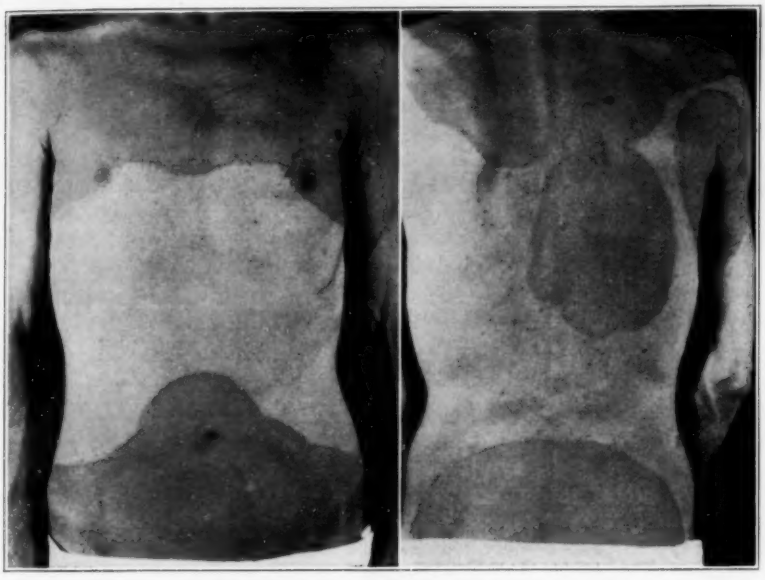

Fig. 1.—Appearance of the patient in August, 1931.

Fig. 2.—Note the peculiar appearance of the palms. In life, there was a lemon-yellow, almost translucent hyperkeratosis.

passed never cleared. For about a year previous to the death of the patient, subcutaneous abscesses appeared on all the involved areas. These ruptured spontaneously and became secondarily infected. Concomitant with heavy alkali treatment, they slowly cleared, only to return about four weeks before death, much more fulminating.

Nearly all the nails were thick, opaque and yellow. The palms were thick and yellow and almost verrucous in places. The tongue was covered with a grayish-white, heavy, shiny, moist coating. The corners of the mouth, the buccal mucosa, the hard and soft palate and as much of the pharynx as could be seen were affected. The whole picture was striking.

Aside from the foregoing findings, nothing abnormal was noted in the physical examination. Medical consultations offered no explanation for the constantly high lymphocyte count. There was never any suggestion of lymphoma from the laboratory or clinical examinations. The blood pressure was 130 systolic and 78 diastolic.

Laboratory Examinations.—The following blood counts were made on three different examinations:

	August, 1930	April, 1931	October, 1931
Hemoglobin	75%		
Red blood corpuscles	3,080,000	4,300,000	4,400,000
White blood corpuscles	12,560	10,000	21,500
Polymorphonuclears	38%	39%	49%
Lymphocytes	56	59	48

It will be noted that the differential count showed a high proportion of lymphocytes, which were variable in size. Blood cultures were consistently negative. On two widely separated occasions, the patient's serum failed to agglutinate his own organisms. The blood sugar and the urine were normal. No yeast organisms were cultured from a sterile specimen. Examination of the stools for occult blood gave negative results. Moniliae were cultivated from the stools in abundance. A roentgenogram of the chest showed one calcified gland at the root of the lung.

Extemporaneous preparations from the tongue and buccal mucous membrane in 40 per cent solution of potassium hydroxide showed a tangled mass of delicate septate mycelia, with an occasional terminal bud. The same was found in scrapings from the skin, though in a lesser degree. The same organism was isolated repeatedly from the mouth, nails and widely separated parts of the skin, and in pure cultures from the subcutaneous abscesses.

Histologic Examination.—Histologically, the characteristic and conspicuous condition consisted of intradermal abscesses lined with giant cells, among which the budding organism was found in profusion.

Mycologic Examination.—The yeast was identified as Monilia albicans. On Sabouraud's maltose agar, it grew as an ivory white, smooth, moist colony, with a definite mycelial down growth in the substratum. In older cultures the center became honeycombed. In gelatin stab cultures the inverted pine tree described by Ashford was formed. It fermented maltose.

Growth was by budding and by the development of septate mycelium. Clusters of spores developed just below the septation, directly from the mycelium or were borne on short hyphae, as noted in figure 5. In old cultures large spherical cells developed (fig. 6) which have been called chlamydospores. When these were picked separately and planted, no germination took place. It seems doubtful that these were true chlamydospores.

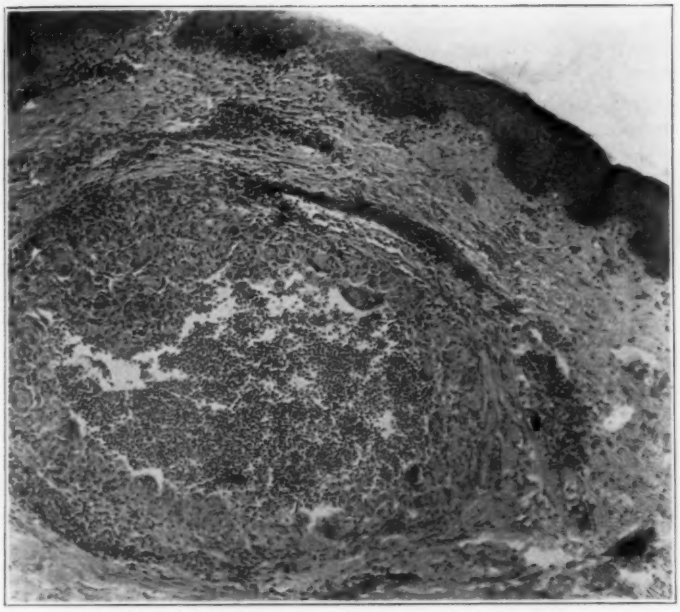

Fig. 3.—Low power magnification of a subcutaneous abscess. The wall of the abscess is made up largely of foreign body giant cells, among which the organism is growing profusely; × 210.

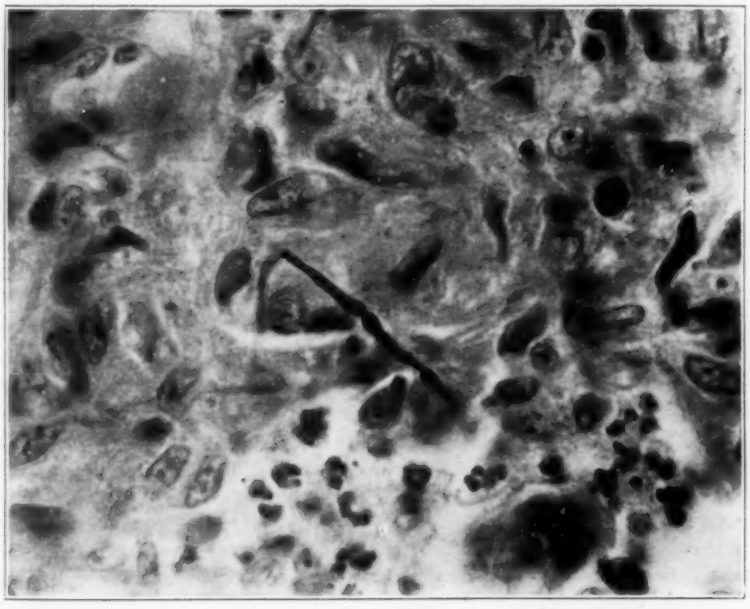

Fig. 4.—Portion of the wall of the abscess showing the infecting organism; × 1,270.

Agglutination with serum from a rabbit immunized against Monilia albicans according to the method of Hopkins and Benham occurred in a dilution of 1:800. Agglutination tests with serums of rabbits immunized against Monilia parapsilosis, Willia anomala and Monilia krusei gave negative results.

The monilia was pathogenic for guinea-pigs when given in doses of 0.2 mg. intravenously. It was recovered from the spleen.

Autoinoculation was done, and a characteristic patch developed, from which the organism was recovered.

Treatment.—Two courses of ethyl iodide were given. Oral medication consisted of the administration of sodium iodide, sodium benzoate and heavy doses

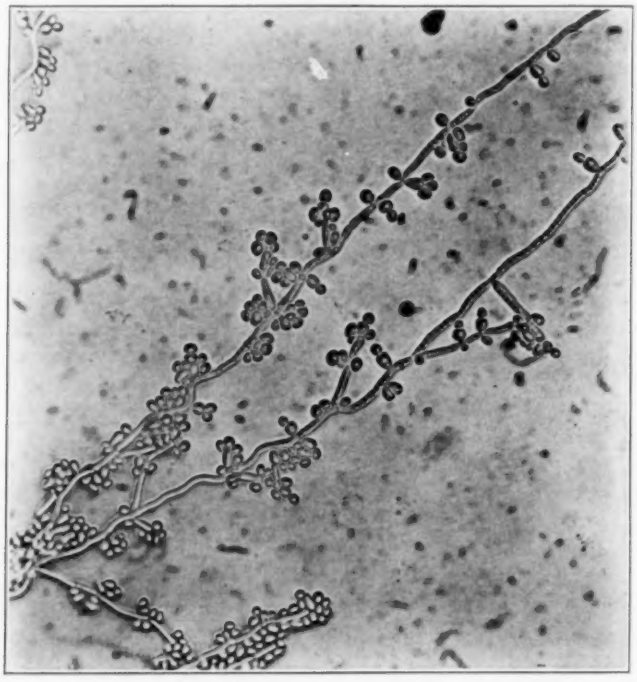

Fig. 5.—A Sabouraud agar block preparation, photographed in a Van Tieghem cell; × 510.

of alkali. Intravenously, the patient was given compound solution of iodine, sodium iodide and neoarsphenamine. Treatment of the oral mucous membrane included the use of sodium perborate, sodium benzoate, potassium chlorate, iodine, potassium permanganate and gentian violet. Topical applications to the skin were made with various fungicidal ointments, such as pyrogallol triacetate and chrysarobin ointments, with various dyes, such as gentian violet, carbol fuchsin and methylthionine chloride, U.S.P. (methylene blue), and with mercurochrome, tincture of iodine and iodine in different bases. The patient also received an autogenous vaccine from which he had no general or local reaction. Heavy irradiation and roentgen therapy produced no improvement. For some time the patient was on a high vitamin diet. It is possible that the ethyl iodide did not have a sufficient trial in this case. Eighteen inhalations of from 1 to 3 cc. each were given in the

first course. The second course was definitely inadequate, owing to the refusal of the patient to continue it.

Autopsy.—Autopsy was performed two and one-half hours post mortem.

The anatomic diagnosis was: generalized monilial infection of the tongue, larynx, esophagus and skin, with secondary infection of the skin; gangrene of the right leg; cachexia; arteriosclerosis, intimal type; anthracosis, and multiple colloid adenomatous goiter (?).

The microscopic diagnosis was: generalized monilial infection of the tongue, larynx, esophagus and skin with secondary infection of the skin; arteriosclerosis, intimal type, and anthracosis.

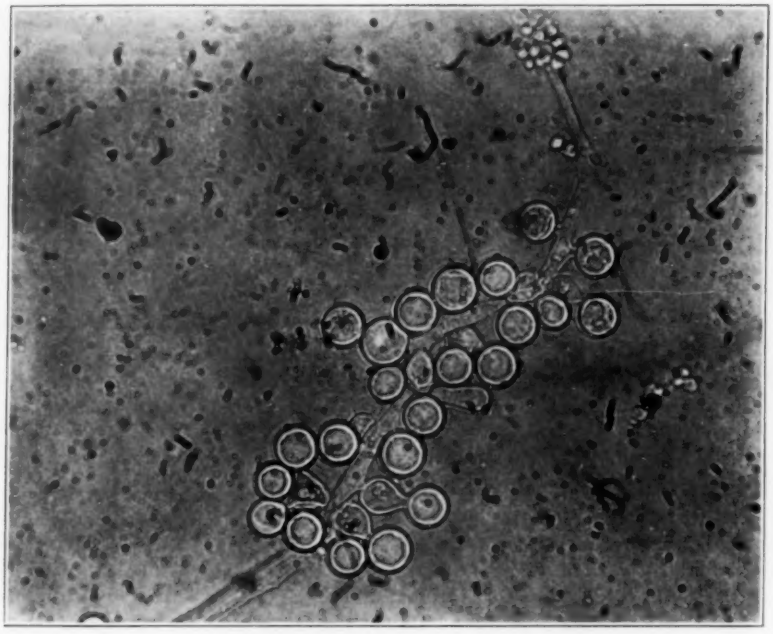

Fig. 6.—So-called "chlamydospores"; × 530.

The body was that of a well developed, much emaciated man. Rigor mortis was moderate and the body was cold. The scalp, face, neck and extremities, except the right leg and foot, and the trunk (but to a lesser extent the upper part of the abdomen and the lower part of the chest) were almost completely covered with cutaneous lesions. Many of the lesions were ulcerated and contained dirty, grayish-yellow pus with a foul odor. Others were covered with a dry, reddish-black crust, on removal of which a fairly thick, yellowish-white pus was revealed. Some lesions were covered with a dry, whitish scale; others were frank pustules, soft, slightly elevated and irregularly shaped. These lesions varied in size from about 0.2 to 1.6 or 2 cm. They were not discrete, and many of them appeared to have fused to form larger lesions. The skin of the right foot was dry, wrinkled, almost hard and dark. The entire skin from the ankle to the middle of the upper third of the leg sloughed off, and a bloody exudate came from the surface. There was a characteristic gangrenous odor.

The ears and nose were normal. The gums were pale and had a foul odor. The tongue was covered with a dirty, grayish-white coating.

Abundant pus exuded into the primary incision from the adjacent skin of the upper part of the chest. There was practically no subcutaneous fat.

The peritoneum was moist and slightly cloudy. There was no free fluid. The intestines were not distended. The liver extended about 7 cm. below the costal margin in the midclavicular line.

The estimated weight of the heart was 225 Gm. The organ was firm, and the endocardium and myocardium were normal. The coronary arteries were normal.

The estimated weight of the spleen was 110 Gm. It was firm, the edge was sharp and there were no scars. On section, it was grayish red.

The estimated weight of the pancreas was 90 Gm. It was normal.

The estimated weight of the liver was 1,700 Gm. It had a smooth surface and was chocolate brown. The edges were slightly rounded. On section, the organ was not remarkable. The gallbladder contained about 15 cc. of black bile.

The suprarenal glands were apparently enlarged, but were otherwise normal.

The estimated total weight of the kidneys was 275 Gm. The capsule stripped easily. On section, these organs were pale. The cortex and medulla were well differentiated. The ureters were normal.

The lymph nodes were slightly enlarged in the mediastinal and lumbar region. The largest one in the mediastinal region was 1.5 by 1 cm.; it was soft and firm in consistency and black. The largest one in the lumbar region was 0.6 by 0.6 cm., and was firm and pink.

The trachea and esophagus were removed intact. The epiglottis and larynx were covered with white coating, similar but less extensive than that on the tongue. This coating also extended for a distance of 11 cm. down the esophagus.

Microscopic Examination.—There was a slight amount of anthracosis in the interstitial tissue of the lungs; otherwise they were normal.

The spleen showed slight intimal thickening of the arteries. A small amount of hemosiderin was found in the pulp.

The gastro-intestinal tract was normal.

A slight amount of fat was seen in the hepatic cells, appearing as small to large droplets throughout.

There were slight fibrosis of the medulla of the suprarenal glands and atrophy of the perisuprarenal fat.

The kidneys showed occasional hyalinized glomeruli and slight interstitial fibrosis with an accumulation of a few lymphocytes.

The bladder, prostate and testes were normal.

The mediastinal lymph nodes showed much fibrosis. A large amount of coal dust and a moderate amount of hemosiderin were found in the interstitial tissue and sinusoids. The node from the mesentery was slightly fibrosed.

The follicles of the thyroid varied in size from medium to very large, the large ones closely approaching the appearance of follicles found in multiple colloid adenomatous goiter. The lining epithelium was of the low cuboidal type. No definite lobulations were seen, but there was slight fibrosis with a few lymphocytes.

A few lymphocytes were seen in the trachea just beneath the epithelium.

A large amount of fibrin and a few polymorphonuclear leukocytes were seen on the surface of the epithelium of the esophagus. In some places the epithelium was sloughed off and in its place could be seen a similar exudate. In other locations the epithelium was much distorted by the presence of fibrin between the cells. An occasional monilia was recognized in the exudate. Beneath the epithe-

lium was an accumulation of a large number of lymphocytes, plasma cells, endothelial leukocytes and a few polymorphonuclear leukocytes. There were a few syncytial masses of endothelial cells resembling giant cells. The blood vessels were engorged and apparently increased in number. The lymphatics contained a large number of polymorphonuclear leukocytes.

The skin contained a considerable amount of fibrosis. Many small abscesses were present, some just beneath the epithelium, and others deep in the subcutaneous tissue. There was much ulceration of the epithelium. The exudate consisted of polymorphonuclear leukocytes, plasma cells, endothelial leukocytes and fibrin and a few giant cells of the foreign body type. Many segments of monilia could be seen, especially in the superficial ulcerated areas.

Summary.—Death was due to the absorption of toxin from the secondary infection superimposed on generalized monilial infection (signed, Shields Warren, M.D.).

A fatal case of infection of the skin with Monilia albicans is reported. Interesting features of the case are:

1. The high percentage of lymphocytes constantly present in the blood. Save in lymphoma we do not know of any other disease of the skin giving a similar blood picture.
2. Repeated isolation of the organism from all the cutaneous and oral lesions.
3. Negative blood cultures.
4. Failure of the patient's serum to agglutinate his own organisms.
5. Failure of all treatment.

Dr. F. B. Mallory and Miss Leavitt made the specially stained slides and Dr. Louis Diches helped in preparing the immune serum.

ABSTRACT OF DISCUSSION

Dr. Cleveland J. White, Chicago: That Monilia albicans can cause a widespread infection in man, with apparently a fatal issue from superficial invasion of the skin, is well proved for the first time. The progressive characteristics constantly involving larger cutaneous areas, in spite of all therapy, are unusual for most Moniliae. We are all willing to accept their usual pathogenic rôle in the causation of superficial infections of the cutaneous surfaces and the mucous membrane of the mouth and vagina. Monilia albicans, when found, is usually pathogenic; other fungi of the Monilia group may be saprophytic. These clinical observations are well substantiated by the recent work of Dr. Benham and by Dr. Stovall.

As emphasized and originated by Weidman, autoinoculation with adequate controls must be used to demonstrate the pathogenicity of Monilia. Animal inoculations are of relative value only. I should like to know more in detail the work that Dr. Greenwood and Dr. Rockwood carried out. The conclusion that the patient died of monilial infection is not absolutely proved. Lack of visceral involvement is most unusual.

While working in Weidman's laboratory at the University of Pennsylvania, I occasionally found that an experimental animal had lesions that could not be observed grossly, and that one had to resort to microscopic examination before

the presence of visceral monilial infection was determined. The kidney was almost constantly involved and occasionally the other organs. In all widespread, localized, undisputed infections due to Monilia albicans, it is wise to check the feces as the source of infection and reinfection.

While the anatomic proof of internal generalization is somewhat inadequate, the agglutination tests strongly support this contention. Consequently we can feel quite sure that the condition reported was a fatal moniliasis, starting from a cutaneous focus.

Dr. Marion B. Sulzberger, New York: It is difficult to come to conclusions as to the effect of Monilia on internal organs. This fungus is usually pathogenic only to the skin and mucous membranes. There is a whole group of these so-called dermatotropic fungi. These organisms, as has been shown experimentally in animals, reach the blood stream and can reside in the internal organs, being found for long periods of time in the liver, spleen, kidneys, brain and other viscera. But in these internal organs they generally cause no lesions. One's general immunity is such that these organisms are not pathogenic in the internal organs. That is why they are called dermatotropic. In Dr. Rockwood and Dr. Greenwood's case there may have been an abnormal lack of resistance on the part of the viscera, particularly in some vital center, in which a small lesion, not discovered at autopsy, may have caused death. There are known cases in which other dermatotropic fungi have done the same thing. Pelerine and Tchernogobouf, six years ago, reported the instance of an entire family in which Trichophyton (ordinarily exquisitely dermatotropic) caused lesions in the cutis, the subcutis, the bones, the viscera and the glands.

Dr. George C. Andrews, New York: I wish to relate a case of a woman who was sent to me two years ago for the treatment of indolent abscesses of the buttocks. Her obstetrician was at the same time treating her for sterility, for she had been married six years and had not been pregnant. Some time after the cutaneous condition was cured, she became pregnant. At the sixth month a pronounced vaginal discharge developed and abortion occurred two weeks later. Cultures from the vaginal discharge and from the placenta showed a yeastlike fungus. Monilia albicans was recovered from cultures of the patient's tongue. The same organism was recovered from the nails and the skin between the toes, and from the vaginal canal, cervix and feces. Monilia albicans recovered from the cervix agglutinated with the patient's serum in a dilution of 1:80. This patient is now being treated by a diet containing large amounts of vitamin B and by injections of liver extract.

Dr. James Herbert Mitchell, Chicago: The fatal outcome in this case is interesting in view of the relative innocuousness of some of these extensive infections. At the recent meeting of the American Dermatological Association I demonstrated a patient who had had an extensive infection for about twelve years. When I first saw her she had erosio interdigitalis saccharomycetica in the third interspace of the right hand, commissural infections, buccal infections, lesions about the breasts, the inguinal folds and the anal region and vulvovaginitis. In addition, she had a severe infection of the interdigital regions of the toes. Cultures were obtained repeatedly from all these areas, including the vaginal mucosa and stools. Simple treatment was instituted, including baths of potassium permanganate, roentgen therapy and treatment with ultraviolet rays from the mercury vapor arc in quartz. There was considerable improvement. When the patient returned in April, 1933, after an absence of three years, she had in addition to the lesions enumerated a psoriasiform eruption about the arms and the trunk.

The only fatality I have had in many cases of moniliasis occurred in a young woman who had vulvovaginitis due to Monilia. Later, a vulvar erosion occurred in which were found abundant bacilli which were probably B. crassus. This case was similar to two reported recently in the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY. The patient in my case was three months pregnant and insisted on an abortion. Her husband took her to a professional, highly successful abortionist in Chicago, but he refused to do anything. She insisted, however, on an operation and succeeded in having it done, but lost her life.

DR. EVERETT S. LAIN, Oklahoma City: My case, which, with the assistance of the research laboratory of Johns Hopkins University, was proved to be one of infection due to Monilia albicans, is even more striking than the case which has been presented by the essayist. The patient, a girl now 18, came to the State University Hospital-Crippled Children's Hospital when she was 12 years of age. The lesions at that time affected the finger-nails and the oral mucosa, with only a few scattered patches over the limbs. The condition has been better and worse during the past six years, almost clearing up at times. Various kinds of treatment have been tried, including the surgical removal of the finger-nails, intravenous treatments and multiple local applications. The most valuable local application thus far found that aids in the removal of the lesions over the limbs and body consists of an ointment composed of 4 per cent salicylic acid and 5 per cent sulphur. The laboratory at Johns Hopkins Hospital prepared a vaccine for this patient which produced marvelous results for a few weeks, but lately it seems to have almost completely lost its potency.

DR. FRED D. WEIDMAN, Philadelphia: This paper concerns a case of monilial infection of the skin with fatal outcome, but it is not quite clear whether it was felt that the death of the patient was due to the infection. I would be much indebted to Dr. Greenwood if he would tell us what the opinion of himself and of the pathologist was regarding this, i. e., whether death was due to Monilia or perhaps to abscesses of the skin resulting from secondary infection.

The lesions are startlingly sharp, as though circumscribed by a pencil line. The distribution is that of dermatomycosis, i. e., intertriginous—bearing out my feeling that such yeast infections of the skin should be classified in the general group of dermatomycosis. These cases of yeast infection always bring up the question of diabetes. Examination of this patient for diabetes gave negative results, but I am still curious to know whether a subdiabetic condition might not exist which would also furnish the "soil" for the development of the lesions. The orange-yellow tint of the hands is something that we all know develops in diabetes; even if a carotinemia can be excluded, the patient may have a high lipid content of the epiderm, such as Schaffer demonstrated in the laboratory at the University of Pennsylvania.

I was intrigued with the shape of the organisms as they occurred in giant cells. In a case of "blastomycetoid granuloma of undetermined nature" which I studied, the configuration of the organisms was strikingly similar to those described by Dr. Rockwood and Dr. Greenwood, and I am indebted for this hint as to their exact nature mycologically.

The study of the feces is important in these cases. Certain yeast fungi are normal flora of the intestine (wild yeasts), but pathogens such as Oidium albicans also parasitize them. The intestinal tract may thus be a reservoir from which the infection may be reseeded onto the skin (recurrences), even though the intestinal tract is free from symptoms. Persistent recurrences of yeast infection around the anus and elsewhere always call for examination of the feces for pathogenic yeasts.

DR. ARTHUR M. GREENWOOD, Boston: I neglected to state that the necropsy reports, both macroscopic and microscopic, failed to show any Monilia except on the skin and extending down the buccal mucosa to the top of the larynx. There was no involvement of any of the internal organs.

In all fatalities there is a primary and contributing cause of death, and it seemed to us and to those who did the necropsy that where abscesses caused by Monilia albicans and containing pure cultures of that organism became secondarily infected it was fair to consider the original infection as the cause of death, although the secondary infection was a contributing cause.

In regard to Dr. Weidman's discussion, studies of the blood sugar were made and the patient never showed more than 10 mg. of sugar per hundred cubic centimeters. There was never at any time a resemblance to the appearance of the skin seen in carotinemia.

The humiliating thing in these cases is that one does not cure the patient. I am inclined to think that by relying exclusively on local treatment we are on the wrong track. As Dr. Sulzberger said, it is a matter of individual resistance. While this patient was under observation, Castle's work on vitamin deficiency in macrocytic anemia was not completed, and although we gave this patient a diet high in vitamins it is possible that the gastric factor necessary for the utilization of the vitamin was absent. If we had given the vitamin intramuscularly, the result might have been different. It may well be that the future treatment of severe monilial infections will be along these lines.

LUPUS ERYTHEMATOSUS (DISCOIDEUS) IN THE TROPICS

FIRST REPORT OF CASES FROM THE PHILIPPINE ISLANDS AND INVESTIGATIONS ON THE OCCURRENCE OF LANGHANS' GIANT CELLS

C. M. HASSELMANN, M.D.
Head of the Section on Dermatology and Syphilology, St. Luke's Hospital Dispensary
MANILA, P. I.

The dermatologic entity which was first described by Biett,[1] in 1828, as "érythème centrifuge" and which was named "seborrhoea congestiva" by Hebra,[2] in 1845, after the dominating clinical aspect, has been known since the report of Cazenave,[3] in 1851, as "lupus erythematosus." Ever since Cazenave's description its pathologic relationship to lupus vulgaris and other forms of cutaneous tuberculosis has focused the interest of dermatologists on this disease.

The scarcity of lupus erythematosus in the tropics in general and among natives in particular led me to report my observations. The case of a native Filipina will be discussed at some length, both on account of its being the first reported case of lupus erythematosus in a native of the Philippine Islands and on account of its interesting pathologic and clinical features.

ETIOLOGY OF LUPUS ERYTHEMATOSUS (DISCOIDEUS)

The parakeratotic scaling, the follicular inflammation and the hypertrophy of the sebaceous glands led Hebra,[2] as already mentioned, to coin the descriptive term "seborrhoea congestiva." This description points also to the often marked hyperkeratosis, which is chiefly noticeable at the mouths of the hair follicles, where horny plugs are formed. The latter phenomenon suggests the elimination of some sort of poisonous substance, analogous to the well known follicular hyperkeratosis in arsenic poisoning.

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1. Biett: Abrégé pratique des maladies de la peau, Paris, 1828.

2. Hebra, F.: Versuch einer auf pathologische Anatomie gegründeten Eintheilung der Hautkrankheiten, Ztschr. d. k.-k. Gesellsch. d. Aerzte zu Wien **1**:34, 143 and 211, 1845.

3. Cazenave: Lupus erythémateux, Ann. d. mal. de la peau et syph. **3**:298, 1851.

The resemblance of lupus erythematosus to lupus vulgaris in a number of gross clinical features and its association at times with coexistent manifestations of tuberculosis of the skin (papulonecrotic tuberculids), lymph nodes, the lungs or other viscera have influenced the French school ever since the time of Boeck and Besnier, Hallopeau [4] and Brocq to uphold emphatically the tuberculous pathogenesis of lupus erythematosus. Arndt, Holder [5] and others succeeded in demonstrating tubercle bacilli in lesions of lupus erythematosus.

A number of cases (Jackson,[6] Bronson, Prospelow, Delbanco) in which lesions of lupus erythematosus disappeared following the removal of tuberculous lymph nodes seem to prove that the presence of tuberculous foci and the presumable production of their poisonous substances may at times be the cause of this dermatologic entity.

Kaposi and others opposed the theory of a tuberculous origin. More recently, however, the members of the Vienna school too (Ullmann [7] and others) have strongly advocated the tuberculous etiology and have stressed the coincidence with other manifestations of tuberculosis. They hold that in lupus erythematosus a fair degree of immunity exists, preventing the appearance of typical tissue tubercles, and that the tuberculotoxins, conveyed through the blood stream, produce lesions of lupus erythematosus on account of a disturbed circulation. Kren and Loewenstein [8] even ventured to state, on the basis of their positive findings, that lupus erythematosus discoideus appears only if there are tubercle bacilli in the blood.

The borderline cases between lupus vulgaris and lupus erythematosus discoideus have been of particular interest to dermatologists. Ravogli even considered lupus erythematosus discoideus only as a variety of lupus vulgaris, the latter affecting the deeper layer of the derma while the former remains limited to the more superficial parts. The pathogenic agent apparently not being sufficient to destroy the implicated tissues to the extent of necrosis, the chronic inflammation and the peculiar degeneration of the connective tissue have led to the superficial yet pronounced atrophy of the skin. This represents one of the leading clinical aspects of lupus erythematosus.

The close relation which exists in some cases between lupus erythematosus discoideus and erythema exudativum multiforme led Galloway

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4. Hallopeau: Semaine méd. **18**:225, 1898.

5. Holder: J. Cutan. Dis. **30**:97, 1912.

6. Jackson, G. T.: A Case of Lupus Erythematosus Changing into Lupus Vulgaris, J. Cutan. Dis. **15**:134, 1897.

7. Ullmann, K.: Arch. Dermat. u. Syph. **78**:372, 1906; Wien. klin. Wchnschr. **22**:1175, 1906; **41**:1159, 1928.

8. Kren and Loewenstein: Arch. f. Dermat. u. Syph. **166**:375, 1932.

and Macleod[9] to consider both conditions as due to toxins of various sorts and of different degrees of virulence, yet as the ends of a chain in which all transitional stages may be encountered, depending on the prevailing stage of circulation in the affected tissues.

The potent circulatory disturbances ever present in lupus erythematosus have brought up the question of an origin in paralysis of the vasomotor nerves. As far as I could ascertain, the only report in support of this conception is that of Biach,[10] who described chronic atrophy of the posterior spinal root ganglions in a case of lupus erythematosus discoideus.

The majority of dermatologists at the present time seem to hold that lupus erythematosus is due to the action of a toxin or toxins involving primarily the capillaries. The frequent symmetry of the lesions points to the causative agent acting through the blood stream. The preference which lupus erythematosus shows for the areas of skin naturally exposed to local trauma is readily explained by the already diminished power of resistance of the respective blood and lymph vessels. The intimate relationship to vascular disturbances is borne out by the frequent connection with chilblain and other vasoneurotic signs of feeble circulation.

It remains for further research to determine whether the circulatory damage of the skin precedes the toxemia. Though the exact nature of the toxin or toxins is not certain, the tuberculous nature of this toxicodermia in many cases has to be rather endorsed than refuted.

The close relationship of lupus erythematosus to lupus vulgaris is discernible from the association of both in the same person (Kyrle[11]) and from the occasionally confusing but identical clinical appearance (Leloir).

The differential diagnosis of the rare transitional cases between lupus vulgaris and lupus erythematosus may become impossible, as the clinical aspect and the histopathologic picture of the same lesion may contradict each other.

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9. Galloway, J., and Macleod, J. M. H.: The Relationship of Lupus Erythematosus and Erythema Multiforme, with an Illustrative Case, Brit. J. Dermat. **20**:65, 1908.

10. Biach, M.: Ueber einen positiven Spinalganglien- und Rueckenmarksbefund bei einem Fall von Lupus erythematodes mit akuten Nachschub, Arch. f. Dermat. u. Syph. **99**:5, 1910.

11. Kyrle, J.: Ueber einen Fall von Lupus erythematosus in Gemeinschaft mit Lupus vulgaris, Arch. f. Dermat. u. Syph. **94**:309, 1909; Ueber eigentümliche histologische Bilder bei Hauttuberkulose und deren Beziehung zum benignen Miliarlupoid (Boeck), ibid. **100**:375, 1910.

CASES OF LUPUS ERYTHEMATOSUS OBSERVED IN THE TROPICS

Admittedly, lupus erythematosus discoideus is rather uncommon in the tropics. However, in the last six years I have seen five cases. In four of them there was no previous history of the malady, which was acquired in the tropics. One case was that of a 72 year old American woman who had had lupus erythematosus of the face several times before in the United States. After an interval of several years she again showed the disease during a longer stay in Egypt and India. It disappeared after treatment with arsphenamine and ultraviolet irradiation but recurred while she was in the Philippine Islands.

Three Japanese, who had come to the Philippine Islands several years before and who had no previous history of lupus erythematosus, after several years of residence showed typical lesions, beginning in the face. Biopsy confirmed the clinical diagnosis.

The last case was that of a girl of the Tagalog tribe, 16 years old, who had never been outside of the Philippine Islands. As this is the first case of lupus erythematosus discoideus reported in a native of the Philippine Islands, it was thought appropriate to study it rather carefully and to give a report of the noteworthy and interesting findings as revealed by clinical and histopathologic study.

The patient said that she had had the lesions "for a long time." She was a well developed girl of healthy appearance. She was never seriously sick. The Wassermann and Kahn reactions were both negative. The blood picture was normal: hemoglobin, 85 per cent; 4,810,000 erythrocytes and 5,600 leukocytes, with 50 per cent polymorphonuclears, 44 per cent lymphocytes, 5 per cent monocytes and 1 per cent eosinophils. The lungs and the urine were normal.

The butterfly wing-shaped lesion was situated over the left buttock and adjacent parts. The center of the affected area showed whitish, depressed scarring. The margin of the lesion was pronounced and markedly elevated. The lesion was purplish red. The peripheral part was made up of partly discrete, rounded, circumscribed papules, about the size of a pea. The tendency to coalesce into patches was marked. There was considerable induration underneath. These efflorescences were not oozing but were covered with greasy, adherent scales. When removed, the scales were found to have typical horny plugs dipping into the dilated mouths of sebaceous gland ducts. These seborrheic, strictly adherent scales formed the peripheral area of inflammatory infiltration, whereas the central parts of the lesion showed characteristic and marked atrophy. There was complete absence of yellowish-brownish staining on pressure with a diascope.

The dermatitis, with the chronicity, the apparent spreading by centrifugal extension, the multiplication of foci at the periphery and the resulting central superficial cicatrices, was typical of lupus erythematosus, as is clearly evidenced by figure 1, though the localization over the buttocks may, perhaps, not be common.[12] This tentative diagnosis became almost certain after the inflammatory

12. Lupus erythematosus over the back has recently been described by a number of observers (Williams, C. M.: Lupus Erythematosus, Arch. Dermat. & Syph. **16**:523 [Oct.] 1927. Walzer, A.: Leukoplaka Buccalis, ibid. **16**:772 [Dec.] 1927) and a case with lesions over the sacrum by S. W. Becker (Lupus Erythematosus, ibid. **19**:506 [March] 1929); Iconog. dermat., Kyoto **4**:22, 1932.

changes cleared up completely following the administration of small doses of quinine by mouth, local painting with tincture of iodine three times a week and the intravenous injection of the disodium salt of 4-sulphonethylamino-2-auromercaptophenyl sulphonic acid. Following the intravenous administration of 3⅓ grains (0.19 Gm.) of the last-mentioned drug, from ⅙ to 1½ grains (0.01 to 0.09 Gm.) being given at weekly intervals, the entire lesion healed with the atrophy characteristic of lupus erythematosus.

Fig. 1.—Lesion over the left side of the lower part of the back and the left buttock, clinically typical lupus erythematosus (discoideus) with no ulceration and with central scarring.

The histologic section, however, was somewhat atypical and necessitated a critical and careful study.

The epidermis was slightly involved, but the main changes were in the corium. The epithelial layer was rather regular and not thickened. The stratum corneum had peeled off in some places; it dipped down into the follicles in other places. There was no tendency to hyperkeratosis in general, except at the mouths of the hair follicles, where the characteristic formation of horny plugs was marked. This was in conformity with the clinical appearance of adherent, plug-carrying scales with stoppage of the follicles.

Fig. 2.—Note the horny plug at the mouth of the hair follicle, the marked edema in the corium with enormous dilatation of the lymph spaces, and the cellular infiltration nodules without necrosis.

Fig. 3.—The pressure in the corium and the edema have led to the formation of lymphatic lakes with a clearly visible lining of endothelium.

There was no evidence of parakeratosis. The stratum granulosum was marked, and in places was enlarged to from four to six layers of keratohyalin-carrying cells.

The prickle cell layer showed acanthosis only in places, and to a very slight degree. There was perhaps a slight diminution of the usual segmentation of the rete pegs, though in other places the interpapillary processes were normal in regard to number and arrangement. The basal layer was well marked and mostly unbroken, though apparently under considerable pressure from underneath. This pressure from the corium proper resulted in detachment of the epithelial layer with formation of the typical so-called *Lymphseen* (lymphatic lakes) of Kyrle.[11] In

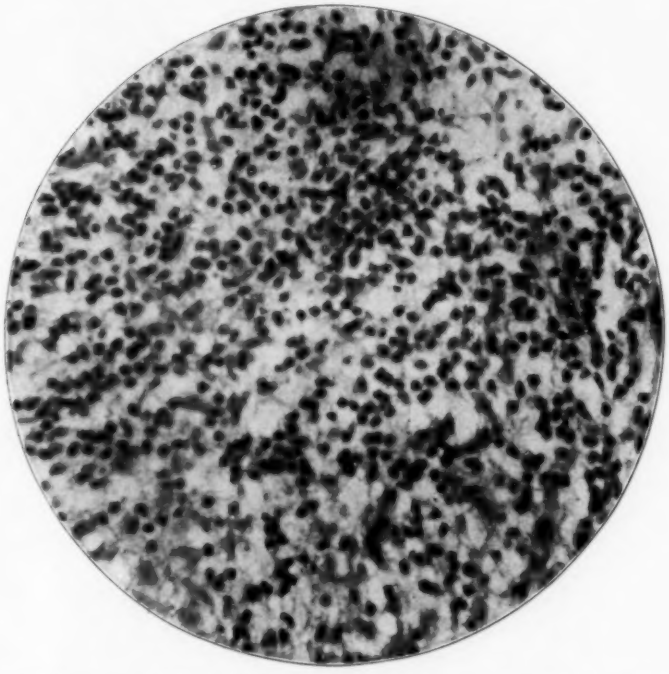

Fig. 4.—The majority of the infiltration cells are lymphoid cells, and the number of spindle-shaped fibroblasts is a sign of a tendency toward healing and repair. Few epithelioid cells are noticeable.

some places the basal layer was obscured by the invasion of polymorphonuclear leukocytes from the cellular infiltration in the corium. This invasion in a few places extended into the middle of the prickle cell layer, though the epidermal surface was nowhere broken, and no ulceration had resulted.

The epidermis also showed marked intercellular and intracellular edema with loosening of the intercellular filamental connections. This marked spongiosis had, furthermore, led in certain places to the formation of the crypts characterisic of lupus-like conditions, with horny pearls of onion shell-like arrangement. Vacuolation of the prickle cells was present in places.

The main changes were in the corium proper. There was, in the first place, an extensive cellular infiltration in the subpapillary layer as well as in the deeper parts

Fig. 5.—Langhans' giant cells are present in small numbers, with magnificent pseudopodia and numerous cluster-like nuclei with a sharply outlined membrane containing large, dark-stained nucleoli.

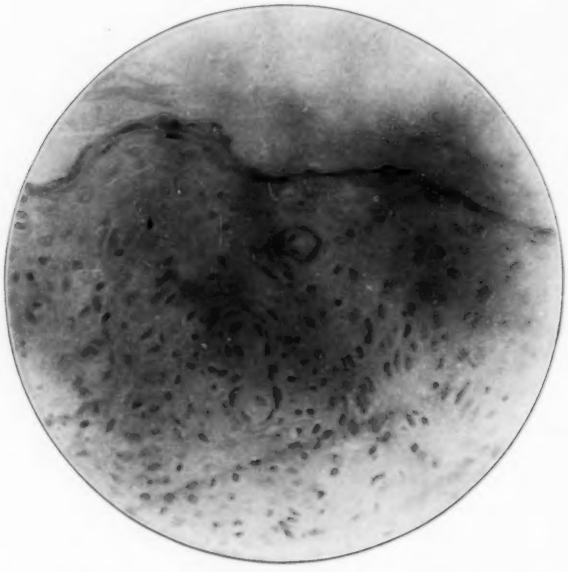

Fig. 6.—The marked spongiosis has led to the formation of the crypts with horny pearls of onion shell-like arrangement.

of the cutis, reaching down to the sweat glands. This infiltration was around and along the blood vessels as well as in distinct, well defined, nodule-like areas. However, absolutely no evidence of necrosis or of caseous formation could be seen. Furthermore, the configuration of the cellular arrangement was uniform, without the characteristic, more or less dense wall of round cells in the periphery that is typical of lupus vulgaris. The cells of the infiltrated areas were of five different types: 1. The majority were dark-stained lymphoid cells. Nearly all were lymphocytes, and only a few showed the characteristics of plasma cells. 2. Spindle-shaped fibroblasts occurred in considerable numbers. They were apparently derived from the fixed connective tissue, as there was marked evidence of fibrosis, showing that the lesions were attempting to heal. 3. The characteristic large epithelioid cells were observed. Their pseudopodia were particularly noticeable, connecting with each other. The resulting formation of a reticulum was clearly visible and distinguishable from the increased fibroblastic changes mentioned. 4. Polymorphonuclear leukocytes were present in very small numbers. 5. As a rather important feature, there were typical Langhans' giant cells disseminated in the reticulum. Some of them were extraordinarily large and showed magnificent pseudopodia. The cluster-like nuclei numbered from thirty to sixty and even more. These nuclei possessed a sharply outlined membrane and rather large, dark-stained nucleoli. Some of the nuclei showed mitotic changes. The giant cells contained a large number of vacuolar enclosures.

In accordance with the observations of Unna and of Fordyce and Holder,[13] I have not found any granular or fatty degeneration of the infiltration cells.

The second dominating feature, besides the perivascular and the tubercle-like cellular infiltration, was the enormous dilatation of the lymphatic spaces, especially in the papillary and subpapillary layers ("central canalization" of Unna). The pressure from the resulting edema had led, in places, to detachment of the epidermis proper from the underlying corium. In others, the formation of so-called *Lymphseen* (lymphatic lakes) with a clearly visible lining of endothelium had resulted. The veins also were dilated. The arteries and arterioles showed very slight traces of proliferation of the intima, but without cellular infiltration. There was no obliteration of the lumens of the blood vessels, thrombosis or endo-angiitis obliterans, as described by Leloir.

The amassment of small blood vessels with capillary qualities suggested that they were young and newly formed. They differed, however, from the vessels of other granulation tissue in that they did not run parallel to each other.

The third principal pathologic feature of the lesion was found in both the collagen bundles and the elastic fibers. They were broken up in many places and showed an irregular, segmented arrangement. In some places they were defective, and in others they were already totally lacking, with resulting atrophy and scar formation.

The sweat glands and the sebaceous glands were normal, except perhaps for slight hyperplasia.

Thus the architecture of the lesion was clearly that of a granuloma with interstitial inflammation and marked evidence of healing and repair. This type of interstitial inflammation has been described by Fordyce and Holder [13] as one of the leading features in lupus erythematosus discoideus. The small round cells, appar-

13. Fordyce, J. A., and Holder, O. H.: Some Clinical Observations on Lupus Erythematosus: The Pathology of Lupus Erythematosus, M. Rec. **58**:41, 1900.

ently lymphocytes, were much more scattered, always with considerable space between and therefore by far less densely accumulated than in other granulomatous inflammations. This phenomenon has been repeatedly described as of pathognomonic value in lupus erythematosus (Kyrle [11]).

COMMENT

Macroscopically, both syphilis and leprosy had to be taken into consideration in the differential diagnosis. A papulosquamous syphilid as well as a gumma could be ruled out on account of the negative seroreactions and the histologic appearance of the lesion. Leprosy, though unlikely in the absence of sensory disturbance, was likewise ruled out both by the absence of Mycobacterium leprae in smears and scrapings from the affected area, and by the histologic picture, which is entirely different from that of leprosy but typical of lupus erythematosus.

At first glance tuberculosis cutis seemed to be ruled out as no apple jelly nodules were detectable on pressure with a diascope. Histologically, the lesion did not possess the characteristics of the usual epithelioid cell tubercle found in lupus vulgaris. Nor did it conform to the entity of "tuberculosis cutis typus Boeck" (Boeck's "benignes Sarkoid" or "Miliarlupoid"), which some authors (Boeck, Kyrle) distinguish from lupus vulgaris on account of the absence of an inflammatory leukocytal wall in the periphery of the usually very large epithelioid cell tubercles.

However, one feature was present in the histologic picture which is common in lupus vulgaris but rather uncommon in lupus erythematosus, namely, Langhans' giant cells.

The presence of giant cells is a matter of great, though not binding, importance in regard to classification. Roth,[13a] in perhaps the most careful and extensive discussion of the subject, which included a report of 250 cases, stated that giant cells of the Langhans' type are occasionally, though seldom, encountered. Such experienced and critical observers as Audry,[14] Darier,[15] Ehrmann, Lenglet, Leredde and Unna also found and reported the presence of Langhans' giant cells in otherwise characteristic lesions of lupus erythematosus. However, the arrangement of the giant cells in the center of a tubercle, typical of lupus vulgaris, is lacking in lupus erythematosus.

A mixed form of lupus erythematosus and lupus vulgaris has been described by Leloir as "lupus érythématoide." Naturally, the question was raised whether cases with giant cells were not such mixed forms

13a. Roth, F.: Ueber die Beziehungen des Lupus erythematosus zur Tuberkulose, Arch. f. Dermat. u. Syph. **51**:3, 247 and 395, 1900.

14. Audry, C.: Bull. Soc. franç. de dermat. et syph., 1894, p. 1071; Ann. de dermat. et syph. **5**:172, 1904.

15. Darier: Lupus erythématodes, in Précis de dermatologie, Paris, J. B. Baillière et fils, 1909.

of lupus erythematosus and lupus vulgaris. Hutchinson, Besnier, Vidal and Lallier have drawn attention to the occurrence of these mixed forms, and have stressed the importance of constitutional, individual and local factors in the pathogenesis and development of the clinical manifestations. This applies also in regard to the histologic feature of epithelioid cells.

Epithelioid cells have been found by various observers, such as Ehrmann and Audry; Ravogli published in his paper photomicrographs showing numerous epithelioid cells. More recently, Freund [16] reported similar observations. However, as Veiel [17] stated in his monograph on lupus erythematosus, nothing resembling the epithelioid cell tubercle typical of lupus vulgaris is found in lupus erythematosus. As the photomicrograph in figure 4 shows, epithelioid cells were present in my case, though they were by no means the dominating type among the infiltration cells.

I waited for over two years before publishing this report in order to eliminate any possible change in the lesions, as lupus vulgaris that in the beginning simulates lupus erythematosus has been repeatedly observed. I am inclined to agree with Jackson that in such cases the erythematous lesions may be due first to toxic infection, and that the manifestation of lupus vulgaris is the result of the tubercle bacilli.

Though one is still compelled to limit the term "tuberculous" to those cases in which Koch's postulate is fulfilled, I believe that the tuberculoid histologic picture of the lesions, at least, was due to toxins closely related to tuberculous infection.

A tuberculin test was not made in my cases, as the diagnostic value of a general or local reaction following any of the tuberculin tests remains inconclusive, the test indicating merely the momentary stage of immunologic defense, allergic or anergic, respectively, as in any other bacteriologic or treponematous malady.[18]

The case reported here shows the fallacy of the statement (Jadassohn,[19] Veiel [17]) that histologic differentiation is always possible without difficulty and doubt. Without fatidical or other sibylline gifts, it cannot be foretold how future research in regard to new staining methods or other achievements may eventually decide the relationship between lupus vulgaris and lupus erythematosus discoideus and their differentiation.

16. Freund, E.: Arch. f. Dermat. u. Syph. **165**:469, 1932.

17. Veiel, E.: Lupus erythematosus, in Jadassohn: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1931, vol. 10, p. 687.

18. Hasselmann, C. M.: J. Philippine Islands M. A., 1928, vol. 35, no. 3; Zentralbl. f. Haut- u. Geschlechtskr. **33**:273, 1930; China M. J. **45**:1131, 1931; Arch. f. Schiffs- u. Tropen-Hyg. (supp. 2) **36**:1, 1932.

19. Jadassohn, J.: Lupus erythematosus, in Mraček: Atlas der Haut-Krankheiten, mit einen Grundriss der Pathologie und Therapie derselben, Munich, J. F. Lehmann, 1899.

The histologic picture in my case would rightly deserve the unbiased diagnosis of granuloma erythematosum, any controversy in regard to lupus vulgaris and lupus erythematosus thereby being excluded. The typical clinical appearance, together with the course of the disease, however, impels me to adhere to the easily understood dermatologic conception of lupus erythematosus discoideus rather than to follow the suggestion of Jadassohn in adopting the diagnosis of granuloma erythematosum.

As Schamberg [20] recently reconfirmed, one type of tuberculosis of the skin may merge into another. Thus, it is a matter of speculation whether the term "lupus vulgaris" *can* be applied only to those lesions with macroscopic evidence of tubercles on diascopy, and *must* be applied as soon as giant cells are found; in other words, whether the presence of giant cells excludes a diagnosis of lupus erythematosus, even if no yellowish-brownish, apple jelly nodules are detectable on pressure with a diascope. I believe that the solution in my case is clear and satisfactory, considering the extreme dilatation of the lymphatic vessels with pronounced subpapillary edema, the predominance of lymphocytes and their peculiar arrangement in the histologic architecture of the tuberculoid nodules, the relative scantiness of typical epithelioid cells, the lack of any noticeable peripheral wall of leukocytes and the absence of any evidence of necrosis but rather the occurrence of fibrosis and a tendency to heal, together with the clinical appearance, the clinical course and the therapeutic effect with complete restitution by typical atrophy and scar formation. All of this, together with the absence of yellowish tubercles in the lesion on diascopy, establishes the diagnosis of lupus erythematosus discoideus with Langhans' giant cells beyond reasonable doubt.

SUMMARY

The first cases of lupus erythematosus (discoideus) from the Philippine Archipelago are discussed.

The first case in a native Filipina is fully discussed in regard to the morphologic picture, the clinical course and the noteworthy histologic picture.

The critical evaluation of these factors eliminates other forms of cutaneous tuberculosis and establishes the diagnosis of "lupus erythematosus (discoideus) with Langhans' giant cells" beyond reasonable doubt.

Though lupus erythematosus is perhaps not quite so common as in the temperate climate, its occurrence in the tropics is by no means exceptional.

20. Schamberg, J. F., in discussion on Weidman, F. D.: Extensive Lupus Erythematosus and Lupus Vulgaris, Arch. Dermat. & Syph. **21**:692 (April) 1930.

Clinical Notes

VANISHING CREAM

ANDREW L. GLAZE, M.D., BIRMINGHAM, ALA.

Greasy ointments and creams which will "vanish" when rubbed into the skin are rare. A cream made as described here will act with such effect when smoothed into the skin in moderate quantities. Its indications suggest themselves. Phenol or the like may be added when desirable.

		Gm. or Cc.
℞	Powdered magnesium carbonate	8
	Solution of calcium hydroxide	16
	Expressed oil of almond	16

Stir briskly before using.

The preparation of a smooth, stable cream from these ingredients is practicable, although even an expert pharmacist may experience difficulty on first trial. The powdered magnesium carbonate is mixed with the lime water; then the required amount of an unadulterated brand of expressed oil of almond is incorporated by slow addition while all are rubbed together in a mortar. Other ingredients may be added after a smooth cream of shiny consistency, without flakes, has been secured.

The vanishing quality of the cream is enhanced by the following modification of the primary formula:

		Gm. or Cc.
℞	Powdered magnesium carbonate	8
	Mucilage of quince-seed with lime	16
	Expressed oil of almond	16

Mucilage of quince-seed with lime is made exactly like the official Mucilago Cydonii, except that solution of calcium hydroxide, U. S. P., is used instead of distilled water.

Biographies

JOSEPH ROLLET, M.D.

B. BARKER BEESON, M.D.
CHICAGO

Martin Pierre Joseph Rollet was born on Nov. 12, 1824, in the little community of Lagnieu in southeastern France. He was the son of the local postmaster. When 9 years old, he entered the nearby seminary of Meximieux. He completed his premedical studies at the Royal College of Lyon, where he won the first prize in philosophy (1842). The same year he began the study of medicine in Lyon, but transferred to Paris two years later. There he distinguished himself by being sixth out of 180 contestants for externships. This high rank secured for him a place in the service of Trousseau at the Hôpital Necker. After only a year of preparation, he became an interne des hôpitaux de Paris in 1845. He spent the allotted three years in the surgical wards, and refused an additional year in order to compete for a place as surgeon-major at Hôtel Dieu, Lyon. He did not succeed in his first concours, although he performed brilliantly, but early in 1850 he won the post as surgeon-major at l'Antiquaille, the oldest and best known Lyonnaise hospital and the seat of the university clinic for diseases of the skin and syphilis. It is worth while knowing that it occupies the site of a sumptuous palace built by Septimus Severus, which later housed the Roman governors. In the fifteenth century, a wealthy native, Pierre Sala, collected the débris of the Roman palace and built a castle with it on the original site. This accounts for its name. Later it became a convent, but since 1795 l'Antiquaille has served as a hospital. A service for diseases of the skin was established there in 1820, and Prosper Baumès, to whom many give equal credit with Colles for the well known law regarding the transmission of syphilis, was the first surgeon-major.

On assuming charge of his service in 1855, Rollet delivered an inaugural discourse which dealt with the contagious agents in diseases

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This biography is based on data in the following works devoted to Rollet: Horand: Notice bibliographique sur J. Rollet, Lyon. méd. **83**:577, 1896; **84**:11, 44 and 84, 1897. Thibierge, G.: L'oeuvre de Joseph Rollet, chirurgien-major de l'hospice de l'Antiquaille à Lyon, de 1855 à 1864. Sa vie (1824-1894), Ann. de dermat. et syph. **5**:609 (Nov.) 1924. This article was read during the celebration of the centenary of the birth of Rollet at Lyon. It is the most extensive sketch of his career. Lacassagne, J.: L'oeuvre de Joseph Rollet, Prophylax. antivén. **4**:261 (June) 1932. This is an unusual biography written by one of Rollet's grandsons who is himself a distinguished dermatologist.

of the skin. He retired in 1865 at the early age of 41, having served the prescribed ten years. The Faculté de Médecine de Lyon was created in 1877, and the chair of cutaneous diseases was given to Gailleton, then surgeon-major at l'Antiquaille and mayor of Lyon. He proved to be an obscure professor and not to be classed with Rollet, who was naturally the logical choice. Rollet was awarded the chair of hygiene, which he held in a truly worthy manner, becoming one of the best known Lyonnaise professors. Rollet received many honors; most of them came tardily owing to his extreme modesty. While an intern, he was most active in caring for the wounded during the insurrection of June 6, 1848. For this he received a medal from the Minister of the Interior with this inscription: "To Citizen Rollet, surgical intern, June 6, 1848." The rank of Chevalier of the Legion of Honor was conferred on him by Empress Eugénie in 1869. Charles Bouchard secured his teacher's election to the Academy of Medicine in 1885, and nine years later, because of his influence, Rollet was admitted to the Institute or the Academy of Sciences. He served as presiding officer of practically all the scientific bodies of Lyon. On the foundation of the French Dermatologic Society in 1889, he was elected one of its honorary presidents, and on the day of his death, Aug. 12, 1894, he was to have presided over a meeting of that body in Lyon.

While at l'Antiquaille, Rollet gave two yearly courses devoted to cutaneous and venereal diseases, which became very popular. On retiring from the hospital in 1864, he gave a noteworthy account of his stewardship. His best known achievement was the recognition of the mixed sore, which problem he is credited with solving as early as 1856. The term "mixed sore," according to Thibierge, was first employed by Laroyenne, one of Rollet's pupils, in his thesis (1858). Rollet also proved the plurality of the venereal disorders, the contagiousness of secondary syphilis and the importance of vaccinosyphilitic contagion as well as of the labial chancre, which he studied in glass-blowers, and also that of the mammary primary lesion, which he noted among wet-nurses. Rollet showed by inoculation that the chancroid could be extragenital. He emphasized the danger of the oral lesions of syphilis, saying, "The mouth is the great laboratory of secondary syphilis." Rollet devoted much time to the study of gonorrhea and its complications, having written about gonorrheal rheumatism, ophthalmia, synovitis and early stricture. Among his dermatologic contributions were: a treatment for scabies; researches on several diseases of the skin reputedly rare or exotic, which should be attached to syphilis; studies on arsenical eruptions and lesions of the skin of persons working with arsenic; studies on the nasal and ocular mucosae; the treatment of psoriasis by mercurous iodide salve and sulphur baths, and a classification of cutaneous disorders founded on their anatomy and etiology.

One cannot refrain from agreeing with Thibierge when he refers to Rollet as the real founder of the Lyon school of dermatology, now so ably represented by Joseph Nicolas and his colleagues. A careful and prudent observer, Rollet deserves a high rank among the outstanding physicians of France. It is no wonder that under such leadership his pupils made excellent contributions to medical literature. Among them may be mentioned, besides Laroyenne: Chabalier, who wrote on the history of venereology; Guyenot, who dealt with the inoculability of syphilis, and Charles Bouchard, who wrote on tinea circinata, pellagra and vaccinia while associated with Rollet. In 1865, Rollet summed up his ideas on the venereal disorders in a volume of about one thousand pages, which is still a classic. Being much concerned with the prophylaxis of venereal diseases, he, along with Crocq of Bruxelles, submitted a noteworthy report on this subject before the International Medical Congress of 1867.

Physically, Rollet was imposing, being tall and strongly built, with heavy eyebrows and a piercing glance. His simplicity and modesty were almost proverbial. He found recreation chiefly in his family.

30 North Michigan Avenue.

Obituaries

R. PROSSER WHITE, M.D.

1855-1934

News comes of the death on Jan. 4, 1934, of Dr. R. Prosser White of England, aged 78. His work on occupational dermatoses has made him so familiar to American dermatologists that in his death we seem to have lost one of our own. His book, with its rapid enlargement in each succeeding edition, has been one of the most useful additions to dermatologic literature of the last twenty years. It has emphasized, perhaps more than anything else since the works of Hebra, the importance of external irritants in the production of dermatoses. It is as much a landmark in its field as the first work on the subject by the great Ramazzini in 1700. The work under the title "The Dermatergoses," which he gave to the last edition, may well be placed beside Ramazzini's "De morbis artificium diatriba."

The following exerpt is from a sketch on Dr. White in the *British Medical Journal* of Jan. 13, 1934, by his colleague, W. E. Cooke:

Dr. Prosser White was a past-president of the London Dermatological Society, of the Manchester Medical Society, and of the Certifying Factory Surgeons' Association, and a member of the Permanent Committee for the Study of Occupational Diseases constituted under the auspices of the League of Nations at Geneva. He was also Associate Editor of the *Journal of Industrial Hygiene*. Outstanding among his contributions to medical literature is the book on "Occupational Affections of the Skin," published in 1915, the fourth edition of which is actually in the press. This work has been translated into every European language, and there have been several American editions. A book full of his own work, it is considered the greatest compilation of facts and references that has ever been published on the subject, and will long remain the standard textbook. In 1930 the Labour Bureau of the United States Government invited Dr. White to deliver a series of lectures on the occupational diseases of the skin, but he felt that the strain on his heart would be too great. Dr. White founded an annual lecture in dermatology, to be delivered by an eminent authority selected each year by the council of the Dermatological Society. His articles on naphthalene, dinitrobenzol, and aniline poisoning, baker's itch, and fur eruptions reveal painstaking work, the conscientious mind, and careful judgment. Only those who knew "Prosser," as he was affectionately welcomed by his friends, realized the amount of work embodied in every article he wrote. His knowledge was wide in the fields both of medicine and of men. With his unbounded energy (although suffering from a cardiac disability for forty years) and his keenness in medicine, it is not surprising that he had no time for the uninterested or the slacker.

"Prosser's" love of that branch of medicine which he chose for his life's work was almost equalled by his love for his native town and its people. About the year

1890 he published a manual for the Church Lads' Brigade Medical Staff Corps, and became principal medical officer and surgeon-colonel of the Brigade, and Editor of the Brigade's "Medical Corps Manual." The proper training of the youth was an essential in his view of life, and he took pains to see that it was done. He was much interested in the Wigan Mining and Technical College, and founded a "French travelling scholarship," whereby Wigan students could spend three months in France, or in any Continental country, to study their special branch. In his younger days the idea of the preservation of records of Wigan led him to commission young artists to paint and make drawings of the old buildings in the town. These are collected in the Public Library. The fifty-fifth picture was added only two years ago. He was also a poet, and several of his poems have been published. His artistic temperament was demonstrated by his interest in music, and this also took a practical and beneficial form; he founded the Wigan Parish Church Musical Fund, for the purposes of insuring an annual organ recital by some well-known organist. In 1924 he founded the Medical Book Trust Fund at the Wigan Public Library. The object of the fund was to buy books on original research in medicine, expensive textbooks, and works in the ancillary sciences. This has been a very valuable and much appreciated branch of the library.

A philosopher, Prosser White's outlook on life is exemplified by his bookplate—a scantily clad man turning away from the lamp of knowledge, the flame of which is a large note of interrogation, and going into the unknown towards the rising sun: the legend is "Why and wherefore." He was a very fine character. Although breezy and cheerful, and going out of his way to help the under-dog, his mind was always on the ultimate good that might accrue from his work.

This is an outline of a great life of a physician who devoted his professional interest and efforts to the help of his fellow man in the manual labor group of society, and who devoted his social interest and his substance to the help of his community. He reminds one of Willan. American dermatologists join their British colleagues in pride in Prosser White.

W. A. P.

Correspondence

"A NEW CUTANEOUS MANIFESTATION IN THE SYNDROME OF VITAMIN A DEFICIENCY"

To the Editor:—With reference to my paper, "A New Cutaneous Manifestation in the Syndrome of Vitamin A Deficiency," which was published in the November issue of the ARCHIVES OF DERMATOLOGY AND SYHILOLOGY (**28**:700, 1933), Dr. Lapa of Lisbon, Portugal, recently informed me that a dermatosis similar to the one I described had previously been reported from China. The reference to this paper is: Frazier, C. N., and Hu, C. K.: Cutaneous Lesions Associated with a Deficiency in Vitamin A in Man (*Arch. Int. Med.* **48**:507 [Sept.] 1931).

LEONARD J. A. LOEWENTHAL, Liverpool, England.

Books Received

CONTRIBUTION À L'ÉTUDE DE LA CALCÉMIE DANS LES TROUBLES DU MÉTABOLISME DU TISSU CONJONCTIF DERMIQUE. Docteur Robert Zorn, Ancien Interne des Hôpitaux de Strasbourg. Pp. 55. Strasbourg: Charles Roch, 1933.

LES MÉDICAMENTS ANTISYPHILITIQUES. F. Henrijean and R. Waucomont. Price, 20 francs. Pp. 186. Paris: Masson & Cie, 1933.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

SQUAMOUS-CELL CARCINOMA OF THE SKIN. BERNARD F. SCHREINER, Am. J. Cancer **19**:829 (Dec.) 1933.

The author reports on 22 patients with squamous cell carcinoma of the skin who were treated prior to 1927 at the New York State Institute for the Study of Malignant Disease, 164 of whom were available for five year statistics. Fourteen patients with mixed basal cell and squamous cell epithelioma were observed. Most of the patients were treated with roentgen irradiation of both low and high voltage and with unfiltered and filtered radium packs. In some instances electrocoagulation and surgical intervention were employed. Treatment with unfiltered x-rays consisted of a single exposure of 2 or 3 erythema doses. Sometimes this was repeated in six or eight weeks. With filtered x-rays the voltage was 200,000, and the filter, 0.5 mm. of copper and 1 mm. of aluminum (the dosage is not stated). Radium treatment was carried out with large amounts of heavily filtered radiation. Of the 156 patients who did not have involvement of the lymph nodes, bones or cartilage, 57 of the 104 available for five year statistics were alive and well after five years or longer; 44 died from progression of the disease and 28 from intercurrent disease. Of the group of 71 exhibiting deep involvement or metastases at the time treatment was instituted, only 4 of the 60 available for five year statistics were recorded as clinically well five years or more afterward, and 53 died from progression of the disease.

EXPERIMENTAL STUDIES ON LYMPHOMATOSIS OF MICE. J. FURTH, H. R. SEIBOLD and R. R. RATHBONE, Am. J. Cancer **19**:521 (Nov.) 1933.

The authors observed that the various clinical types of lymphomatosis (lymphoid leukemia, lymphosarcoma, etc.) depended on the character of the malignant lymphocytes and whether or not they had free entrance to the circulation. They differentiated malignant lymphocytes from lymphoblasts. They found the disease to be transmissible to healthy animals, success of transmission depending on the transfer of healthy cells, and they recognize an inherited susceptibility of the host.

THE ETIOLOGICAL AND PATHOLOGICAL ASPECTS OF SQUAMOUS-CELL CARCINOMA OF THE PENIS AMONG THE CHINESE. S. K. NGAI, Am. J. Cancer **19**:259 (Oct.) 1933.

Studies made at the Peiping Union Medical College indicate that among the Chinese cases of cancer of the penis constitute more than 18 per cent of all recorded cases of cancer, as contrasted to 5 per cent in continental Europe, 1.27 per cent in Great Britain and 2 per cent in the United States. The disease was found to be most prevalent among farmers and coolies, the former comprising 41 per cent of the patients, and to occur about a decade earlier than among Western people. Practically all of the tumors studied appeared to have had their origin in the epithelium of the coronal sulcus or of the inner surface of the prepuce.

It is assumed that this high regional incidence of penile cancer is attributable to lack of personal hygiene and to the limited practice of circumcision, both of which favor epithelial irritation from smegma. It is significant that a history of phimosis was recorded in 99 per cent of the cases, that venereal disease appeared to be an insignificant factor and that no case was observed in a person who had undergone circumcision early in life. Of fifty-two cases in which the inguinal nodes were sectioned, only seventeen showed metastatic growths, the enlargement of the nodes in the others being inflammatory; internal metastasis was uncommon.

FOERSTER, Milwaukee.

A Report on Instruction Regarding Syphilis in American Medical Schools. M. J. Exner, Am. J. Syph. **17**:449 (Oct.) 1933.

By means of a questionnaire sent to various medical schools, Exner sought to ascertain the extent of the attention given to syphilis in the students' curriculums. The answers received indicate that there exists a wide range of variation between the best and the worst in the extent and thoroughness with which the subject is taught.

A study of the reports of the groups of schools which are doing the most thorough work in the teaching of syphilis reveals certain features which they have in common: Syphilis is taught as a special subject so as to be presented with unified completeness and coordination of subject matter. The subject is also taught in its pertinent relations to dermatology, neurology, pediatrics and other subjects. It is taught mainly in the third and fourth years; some laboratory aspects may be presented in the second year. The teaching is diversified into class lectures, class or group demonstrations and seminars; there is extensive study of cases in clinics by small groups under supervision. Demonstrations of the technic of dark-field examination and of intravenous and intramuscular injections are given and practice is provided for. An understanding of the principles involved in the serologic tests is given, with interpretation of the results. There is instilled in students an appreciation of the importance of accurate and adequate case histories and of the need of developing an epidemologic and sociologic as well as a clinical point of view in relation to syphilis. An average of at least sixty-eight hours is devoted specifically to syphilis.

Congenital Syphilis. Advantage of Early Treatment as Judged by the Wassermann Test. L. Chargin and M. Umansky, Am. J. Syph. **17**:468 (Oct.) 1933.

The records of 134 infants and children with congenital syphilis treated in the outpatient department of Mount Sinai Hospital during the past twelve years were studied. The patients were treated for the most part by alternating injections of neoarsphenamine with injections of preparations of mercury or bismuth given in courses. With the Wassermann test as the criterion this study indicates that in congenital syphilis the best results are obtained when therapy is instituted very early in life.

Meaning and Reliability of Umbilical Cord Wassermann Tests. J. Roby and P. A. Lembcke, Am. J. Syph. **17**:473 (Oct.) 1933.

Roby and Lembcke present some rather startling conclusions: The Wassermann reaction of the blood of the umbilical cord reflects almost exactly the condition of the mother's blood at the time of labor. If the reaction of the mother's blood is negative, that of the blood in the cord will be negative; if it is positive, that of the blood in the cord will be positive. The substance causing the positive Wassermann reaction passes out of the child's blood in most cases before the end of two months, leaving the blood with a negative reaction, provided the child does not have syphilis. If the child has syphilis, after days or weeks the Wassermann reaction of its blood will remain as strongly positive as was that of the blood of the cord. A descending curve of positiveness in Wassermann reactions means that the child does not have syphilis, and treatment should be withheld!

Most of the children and many of the mothers were treated with sulpharsphenamine intravenously, and the authors conclude that sulpharsphenamine may be regarded as one of the most innocuous antisyphilitic drugs now in use; its lack of toxicity is most marked in comparison with its high efficacy.

SYPHILITIC ORIGIN OF ELEPHANTIASIS OF THE VULVA. J. T. WITHERSPOON, Am. J. Syph. **17**:499 (Oct.) 1933.

Twenty-six cases of elephantiasis of the vulva from the records of Charity Hospital, New Orleans, were analyzed. All the cases occurred in colored women. In nearly three fourths of the cases syphilis could be demonstrated clinically or serologically, and in practically the same proportion ulceration was a factor, the portal of entry for the infection thus being evident. Witherspoon discusses the etiology, the pathology and the clinical consideration of elephantiasis in general. The symptoms, physical findings, mode of treatment and immediate results in twenty-six cases are reported.

FIXED DERMATITIS DUE TO TRYPARSAMIDE. H. M. ROBINSON, Am. J. Syph. **17**:507 (Oct.) 1933.

Robinson describes a typical "fixed" eruption apparently due to tryparsamide. The drug has heretofore never been reported as causing this type of eruption. The patch test with tryparsamide was negative both in the involved and in the uninvolved areas.

THE CELLULAR PATHOLOGY OF EXPERIMENTAL SYPHILIS AS STUDIED BY THE SUPRAVITAL METHOD. R. S. CUNNINGHAM, H. J. MORGAN, E. H. TOMPKINS and S. HARRIS, JR., Am. J. Syph. **17**:515 (Oct.) 1933.

By means of the supravital method of staining, the lesions of experimental syphilis in the rabbit were found to contain large numbers of phagocytic mononuclear cells (clasmatocytes, macrophages). These cells were much more numerous than in the same tissues in normal animals and were also greatly stimulated in their capacity to phagocytose. Epithelioid cells of the type seen in tuberculous lesions were rarely seen, suggesting that the reactions of the tissue are quite different in the two conditions.

EFFECT OF TRYPAN BLUE ON EXPERIMENTAL SYPHILIS IN THE RABBIT. H. J. MORGAN, S. HARRIS, JR., E. H. TOMPKINS and R. S. CUNNINGHAM, Am. J. Syph. **17**:522 (Oct.) 1933.

There is evidence in the literature that trypan blue intravenously injected induces a marked increase in the production of phagocytic mononuclear cells (clasmatocytes) and stimulates their phagocytic activity. Syphilitic lesions in rabbits treated with trypan blue underwent resolution more rapidly than those in untreated animals. When rabbits were given trypan blue coincidentally with the inoculation of Spirochaeta pallida the period of incubation was markedly lengthened. As trypan blue is not spirocheticidal it is suggested that this substance modified the course of experimental syphilis in rabbits by increasing the number and activity of the phagocytic mononuclear cells.

RUETER, Milwaukee.

SKIN LESIONS OF PELLAGRA: AN EXPERIMENTAL STUDY. T. D. SPIES, Arch. Int. Med. **52**:945 (Dec.) 1933.

Ten persons with pellagra having a typical dermatitis but no neurologic manifestations were put on a "pellagra-producing" diet of corn-starch and lactose.

Eight of these patients tolerated the diet and began to show improvement within fifteen days after the experiment was begun, even though they lost weight and strength at the same time.

Six albino rats fed on this diet at the same time died within four weeks.

Two patients could not tolerate the diet.

The writer thinks it possible that the specific chemical substance related to the development of the pellagrous dermatitis may be different from that affecting manifestations of the disease in the gastro-intestinal tract and the central nervous system.

UNCOMPLICATED SYPHILITIC AORTITIS: DIAGNOSIS, PROGNOSIS AND TREATMENT. J. E. MOORE and P. F. METILDI, Arch. Int. Med. **52**:978 (Dec.) 1933.

Seven diagnostic criteria of uncomplicated syphilitic aortitis are given. The presence of two or more of these in a person with a late stage of syphilis without disease of the mitral valve gives support to the diagnosis.

One hundred and fifteen patients in whom a diagnosis of uncomplicated syphilitic aortitis was made were studied; all of them were definitely syphilitic and had at least two of the seven diagnostic criteria. The average period of observation was eight years.

In 19 per cent of this group graver forms of cardiovascular syphilis subsequently developed, this tendency being more pronounced in the poorly treated patients. Efficient treatment was shown to relieve symptoms, prevent severe symptoms and prolong life; treatment was much more effective before the development of regurgitation or aneurysm.

Complicating hypertension doubled the mortality and the incidence of the severe types of cardiovascular syphilis.

JAMIESON, Detroit, Mich.

LUPUS ERYTHEMATOSUS BEFORE PUBERTY. D. TRUETT GANDY, Arch. Pediat. **50**:652 (Sept.) 1933.

Two cases of lupus erythematosus in brothers, aged 12 and 13 years, are reported. This disease has always been regarded as rare in infancy and childhood, but a critical study of recorded cases reveals an incidence of about 5 per cent. In view of many unreported and unrecognized cases the actual percentage is doubtless higher. Pediatricians are urged to be on the alert for this disease.

AUTHOR'S SUMMARY.

AN INVESTIGATION ON THE DIAGNOSTIC VALUE OF SERUM PROTEIN CHANGES IN KALA-AZAR. M. R. G. MUDALIYAR, S. K. SUNDARAM and A. S. RAMACHANDRAN, Indian J. M. Research **21**:361 (Oct.) 1933.

The authors conclude that estimations of serum protein cannot establish a diagnosis of kala-azar but that they are of real help when considered with other evidence, even when the formol-gel test is negative.

They were unable to determine how early in the course of the disease the serum protein content changes sufficiently to be a diagnostic aid.

JAMIESON, Detroit, Mich.

PROGRESSIVE LETHAL GRANULOMATOUS ULCERATION OF THE NOSE. J. P. STEWART, J. Laryng. & Otol. **48**:657 (Oct.) 1933.

Stewart describes a disease for which there is no definite name and the cause of which is obscure. In his opinion, the most descriptive term is "progressive lethal granulomatous ulceration of the nose." Ten cases of this disease are reviewed. It is practically confined to the male sex, the ratio being 9:1. Eight of the ten cases occurred in persons between the ages of 28 and 42 years. The pathologic basis is unknown. From the clinical and microscopic appearances, the author concludes that the condition is not a tumor but essentially a pyogenic disease, a chronic inflammatory process. "Malignant granuloma" is an unjustifiable designation. He finds no connection between this disease and Hodgkin's lymphogranuloma. It is a process, not of formation, but of destruction, while the presence of granulation tissue may justify the term "progressive granulomatous ulceration." The clinical picture is one of progressive destruction of the nose, face and pharynx. It is characterized by a mild leukocytosis (14,800), or a leukopenia (2,200), with the white blood cells in normal proportions. There are prolonged and hectic fever and frequent and severe hemorrhages. The duration of the illness is from one to two years. The most marked feature is the complete absence of resistance to the

infection on the part of the patient. It must be differentiated from ulceration occurring in the nose due to the following diseases: syphilis, tuberculosis, cancer, agranulocytosis, mycosis, myiasis, yaws or frambesia, leprosy, rhinoscleroma, leishmaniasis, gangosa and trophic postencephalitic ulceration. In six of seven cases, when bacteriologic findings were given, the presence of both a streptococcus and a staphylococcus was reported. As regards treatment, local applications proved unavailing. Treatment with radium was employed in two cases with indefinite results, but high voltage roentgen therapy promised more success and deserves further trial. Eight patients died of the direct effects of the disease, namely, sapremic cachexia and repeated hemorrhage. One survived for four months after local cure before succumbing to generalized sarcomatosis cutis, and one died from atypical "miners' phthisis" four years after recovery from the local condition. A review of ten cases, reports of which were collected from the literature, is appended.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

FURTHER OBSERVATIONS ON MICROCOCCUS MYCETICUS AND MICROCOCCUS METAMYCETICUS. A. CASTELLANI, J. Trop. Med. & Hyg. **36**:249 (Sept. 1) 1933.

In this article Castellani details the cultural characteristics of Micrococcus myceticus and also gives the staining reactions.

The lesions produced on the human skin resemble streptotrichosis or nocardiosis, small abscesses being present which burst after a long period, with subsequent development of sinuses.

The disease is ushered in by the appearance of a red, raised area from 2 to 3 cm. in diameter, accompanied by a rise to 104 F. in temperature. The temperature soon subsides, but the spot persists, and other similar areas develop. These patches become thickened, nodular and suppurative, with formation of sinuses.

The morphology and the staining reactions of a similar organism, Micrococcus metamyceticus, are also described.

This organism was found in cases of nonfilarial elephantiasis.

Further details will be published later.

THE SYMPTOMATOLOGY OF YAWS IN LIBERIA: III. GOUNDOU AND GANGOSA, G. W. HARLEY, J. Trop. Med. & Hyg. **36**:252 (Sept. 1) 1933.

This study gives in tabulated form the relation of goundou and gangosa to the other symptoms of yaws. The writer believes that the evidence justifies the conclusion that these two conditions are closely related and that both are manifestations of yaws in Liberia.

JAMIESON, Detroit, Mich.

AGGLUTINATION IN VARICELLA. C. RUSSELL AMIES, Lancet **1**:1015, 1933.

The observation by Aragao and Paschen that elementary bodies are present in the fluid of the vesicles of varicella has been amply confirmed. A method of preparing purified suspensions of these bodies is described. In such suspensions the bodies are specifically agglutinated by the serum of patients convalescent from varicella. The results obtained in a series of sixty-one agglutination tests are recorded. The constant presence of the elementary bodies in the fluid of the early vesicles and the fact that they are specifically agglutinated by the homologous antiserum are regarded as strong evidence in favor of the view that these represent the infecting agents of varicella.

AUTHOR'S SUMMARY.

MODERN CONCEPTIONS OF HEREDITARY SYPHILIS. M. CARLE, Ann. de dermat. et syph. **4**: 106 (Feb.) 1933.

Syphilographers are now almost unanimous that the mother of a new-born syphilitic baby is always syphilitic, and that her seeming ability to nurse such an infant with impunity is due to the fact that she is "protected by her own syphilis"; they also believe that an infant born of a syphilitic mother is habitually syphilitic in spite of appearances of health.

A few authorities admit the occasional possibility of an inheritance of syphilitic contamination directly from the father, but all recognize that this is very rare. Carle believes that paternal transmission of the spirochete to the ovum does not occur.

The presence of the spirochete in the semen does not by any means favor the possibility of paternal transmission. The semen is a complex fluid into the composition of which secretions from several different sources enter (e. g., prostate and seminal vesicles). A syphilitic lesion of one of these organs easily explains the presence of the spirochete in the semen, and this readily accounts for the frequence of chancres on the vagina and cervix, at the same time refuting the idea of conceptional syphilis of paternal origin.

There is no possible explanation of paternal transmission except a supposition that the spirochete, lodged in the spermatozoon, penetrates with it into the ovum. Two objections to this theory are apparent. First, the spirochete is three or four times larger than the head of the spermatozoon, and there is no record of any one ever having seen the one in the other. Second, it seems inconceivable that the infection of the spermatozoon, transmitted to the ovum in turn, could permit the development of so delicate an organism as the fetus.

Of course, it has been postulated that the spirochete may penetrate the spermatozoon in an ultramicroscopic granular form and subsequently undergo normal development. But it is far more logical to assume that the spirochete infects some point in the maternal genitals, perhaps at the same time that the spermatozoon fertilizes the ovum, whereupon the contaminated mother transmits the disease to the fetus by the hematogenous route.

FOLLICULAR SYPHILIDS. MILIAN, Bull. Soc. franç. de dermat. et syph. **40**:210 (Feb.) 1933.

Milian believes that tuberculosis plays a rôle in the development of the follicular type of syphilid. He advances the following arguments: 1. The follicular syphilid does not differ clinically from lichen scrofulosus. 2. Histologically the lesions of the two conditions are similar. 3. A tuberculin test in the presence of miliary lichenoid syphilids gives not only a general and a local reaction, proving the existence of tuberculosis in the patient, but also a focal reaction in the lesions themselves, indicating their tuberculous nature.

CHANCRE OF THE CONJUNCTIVA OF THE UPPER EYELID. BERTIN, CHRISTIN and LESENNE, Bull. Soc. franç. de dermat. et syph. **40**:213 (Feb.) 1933.

Apparently chancre with this localization has never been reported before. The lesion occupied the under surface of the upper lid, not the free border as usual. A small, painless, slightly indurated tumefaction of the lid was visible from the outside, and on turning the lid back an oval ulcer was seen. There was preauricular and submaxillary adenopathy. On further examination a papular secondary eruption was found; the Wassermann reaction of the blood was positive. The patient was 8 years of age. The method of inoculation is unknown.

RINGWORM IN AN ADULT DUE TO MICROSPORON FELINEUM. SÉZARY and GEORGES-LEVY, Bull. Soc. franç. de dermat. et syph. **40**:218 (Feb.) 1933.

A case of ringworm of the scalp in an adult is reported, Microsporon felineum being indicated as the causative organism. The infection came from a domestic cat.

ANNULAR SYRINGOCYSTADENOMA OF THE FOREHEAD. SÉZARY and LEVY-COBLENTZ, Bull. Soc. franç. de dermat. et syph. **40**:224 (Feb.) 1933.

A man, aged 44, presented an annular lesion on the forehead in the diagnosis of which it was impossible to decide clinically between granuloma annulare, annular lichen planus and epithelioma. Biopsy showed the condition to be syringocystadenoma.

GENERALIZED EDEMA CONSECUTIVE TO INTRAVENOUS INJECTION OF SODIUM THIOSULPHATE. NICOLAS, PETOURAUD and VIAL, Bull. Soc. franç. de dermat. et syph. **40**:362 (March) 1933.

Generalized edema suddenly developed in a patient receiving sodium thiosulphate intravenously. This was believed to be due to the drug. After subsidence of the edema the treatment was continued without further untoward incident.

DARIER'S DISEASE. LOUSTE, RABUT and RACINE, Bull. Soc. franç. de dermat. et syph. **40**:398 (March) 1933.

A typical case of Darier's disease is reported. An unusual feature was the repeated outbreaks of secondary pyodermic infection among the dyskeratotic lesions. A similar condition existed in the patient's mother, the onset in her case dating from the twelfth year of life, while in the patient the disease began at the age of 19.

PITYRIASIS VERSICOLOR IN A NEGRESS. GOUGEROT, P. BLUM and J. MEYER, Bull. Soc. franç. de dermat. et syph. **40**:420 (March) 1933.

Gougerot, Blum and Meyer assert that this case of pityriasis versicolor in a Negress confirms the hypothesis advanced by them in 1929, that the white spots produced by this condition represent true hypochromia due to an alteration of the pigmentary function of the skin and are not normal skin seemingly discolored by contrast.

TREATMENT OF VITILIGO WITH OIL OF BERGAMOT IN COMBINATION WITH ULTRAVIOLET RAYS. LOUSTE and JUSTER, Bull. Soc. franç. de dermat. et syph. **40**:428 (March) 1933.

In a patient with vitiligo of four or five years' duration an esthetic result was obtained with the well known treatment by oil of bergamot in combination with ultraviolet rays.

ACTION OF LARGE DOSES OF AN EXTRACT OF HOG'S SPLEEN IN CERTAIN DERMATOSES. PASTEUR, VALLERY-RADOT and BLAMOUTIER, Bull. Soc. franç. de dermat. et syph. **40**:506 (April) 1933.

Results from the use of an extract of hog's spleen in the treatment of several dermatoses are reported. An injection was given intramuscularly every day for twelve days and every other day thereafter. Each dose corresponded to 50 mg. of fresh spleen.

In thirty-seven cases of eczema results were good in sixteen, fair in eight, temporary in seven and nil in six. Oozing and weeping types responded best, and pruritus was relieved. In twenty-eight cases of urticaria results were good in seven, fair in five, temporary in eight and nil in eight. Cases of dietary origin responded best. Those due to physical allergy did not respond. In one case of Quincke's edema and in one case of psoriasis the disease was checked. Large doses must be used to be effective, and the treatment is most successful in moist eczemas.

GANDY, Houston, Texas.

EPITHELIOMAS OF THE LIDS AND THEIR TREATMENT BY RADIUM. S. LAVORDE, Presse méd. **41**:1548 (Oct. 7) 1933.

Of 676 cutaneous cancers recorded at the Cancer Institute since 1921, 84 or 12.4 per cent were epitheliomas of the lids. Histologically, 37 were of the basal cell type; 29 were classified as intermediate and 12 as spindle cell type. In 6 cases histologic examination was not practical. The technic of the application of radium is outlined in detail. Of the 84 epitheliomas, only 56 were treated, the others being eliminated because (*a*) 16 were perforating in type, (*b*) 3 had invaded the globe, (*c*) 3 were treated with electrocautery, (*d*) 2 were excised surgically

and (*e*) 4 occurred in patients who would not submit to treatment. Of the remaining 56, 50 were destroyed.

Lavorde believes that radium, properly used, is the ideal therapeutic agent, as it causes no deformity of the lids, no lesions of the globe and no late accidents.

MAYER, [ARCH. OPHTH.]

PRODUCTION OF TUMOR-LIKE GROWTHS BY INORGANIC SALTS. ERNST LEUPOLD, Beitr. z. path. Anat. u. z. allg. Path. **89**:542, 1932.

Small papillomas were produced on the tongues of rabbits by injecting into the tissue hypotonic saline solutions. Simple washing of the oral cavity was also effective. The most potent substances were calcium chloride and sodium chloride. When the same substances were injected near artificial wounds in the ears of rabbits, fibroma-like growths appeared in the healing wounds. These tumor-like growths were not autonomous but disappeared spontaneously after cessation of the irritation. Disturbance in the salt concentration of the tissue is regarded by Leupold as an important factor in the etiology of neoplasms.

HELLWIG. [ARCH. PATH.]

EXPERIMENTALLY INDUCED EPITHELIAL PROLIFERATION OF THE RABBIT'S TONGUE. W. RONDORF, Beitr. z. path. Anat. u. z. allg. Path. **91**:176, 1933.

This is a contribution to the conceptions of Leupold, under whose direction the work was done, concerning the effect of local cellular metabolism, as influenced by certain organic and inorganic substances, on cellular proliferation. The substances used in these experiments were calcium chloride and potassium chloride in solutions of 1:1,000,000 strength, and leucine, glycogen and cholesterol, mostly in solutions of 1:1,000,000 and 1:10,000,000. The quantity injected just beneath the epithelium of the margin of the rabbit's tongue was 0.05 cc. This quantity and the strengths of the solutions are reminiscent of the homeopathic procedure of "proving" drugs. The injections were repeated at intervals of from two to eight or ten days. Judged by the size and number of papillomas that developed, calcium chloride, leucine, glycogen and cholesterol were most effective; next most effective were potassium chloride and cholesterol plus one or another of the salts, and least effective were water and cholesterol in concentrations of from 1:100,000 to 1:1,000. The findings are discussed in the light of Leupold's speculations.

SCHULTZ. [ARCH. PATH.]

ONYCHIA AND PARONYCHIA DUE TO FUNGI OF THE YEASTLIKE TYPE: THEIR PATHOGENIC IMPORTANCE. EUGENIO TARANTELLI, translated by HEINZ RANZENHOFER, Dermat. Wchnschr. **97**:1311 (Sept. 9); 1346 (Sept. 16) 1933.

The author reviews briefly the literature in regard to infections with Monilia and allied organisms. Six cases of onychia and paronychia are described, with the cultural findings. Attempts to determine the presence of antibodies by complement-fixation and agglutination tests failed. In three of the six cases intracutaneous tests were positive. The pathogenicity of Monilia is discussed, and the conclusion is reached that it may be definitely pathogenic. The diagnosis and treatment of these infections are dealt with briefly.

TAUSSIG, San Francisco.

Society Transactions

LOS ANGELES DERMATOLOGICAL SOCIETY

NELSON P. ANDERSON, M.D., *Secretary*

Regular Meeting, Oct. 10, 1933

STANLEY O. CHAMBERS, M.D., *in the Chair*

DARIER'S DISEASE. Presented by DR. THOMAS NISBET.

F. R., a white man, aged 31, states that in September, 1926, an erythematous eruption appeared suddenly on his abdomen. The eruption rapidly became generalized and assumed its present appearance.

During the four years following the onset, the patient was treated in various naval hospitals and aboard ship, receiving a large number of injections of neoarsphenamine as well as local treatment, without result. He has had numerous Wassermann tests, all of which were negative.

He presents a generalized eruption consisting of large papules covered with an adherent, greasy, gray crust. The scalp is covered with similar greasy scales.

DISCUSSION

DR. C. R. HALLORAN: I have seen two patients with Darier's disease at the Los Angeles County General Hospital. I gave each patient a course of twenty injections of gold and sodium thiosulphate. One patient improved temporarily, but with further medication improvement did not continue.

ACNE ROSACEA TREATED WITH AN ALKALINE SULPHUR OINTMENT. Presented by DR. NELSON P. ANDERSON.

This man, aged 45, was first seen on April 26, 1933. He had been troubled with an occasional "pimple" on his face for several years. About two years before I saw him he began to have more lesions on his face, particularly on the cheeks and over the nose. A dermatologist gave him twelve roentgen treatments, and his face became fairly clear and remained so for three or four months. About January, 1933, the condition recurred. Following its recurrence, he was given six or seven intramuscular injections of corrosive mercuric chloride, ⅛ grain (0.008 Gm.). He had always been constipated.

On April 26, 1933, he presented marked acne rosacea. Examination of the follicular plugs under the microscope revealed no parasite. Examination of the pus from the pustules revealed several mites (Demodex). A Kahn test of the blood was negative.

An alkaline sulphur ointment was prescribed for local use. Three days later the patient was a great deal better in spite of the fact that a severe local reaction with much crusting followed the use of the ointment. At this time, dressings wet with compound solution of copper and zinc sulphate (Alibour's solution) were prescribed. On May 3, the reaction had practically subsided, and he was advised to use the alkaline sulphur ointment for two nights. A severe reaction with crusting again followed its use, and dressings wet with compound solution of copper and zinc sulphate were applied. By the middle of May, his face had cleared remarkably and the pustules had practically disappeared, although there was considerable redness of the involved areas.

DISCUSSION

DR. SAMUEL AYRES: The eruption was so severe that the patient did not leave his room even for meals. I think that this case is a striking example of a therapeutic result. The roentgen treatment which the patient received prior to consulting Dr. Anderson was without benefit. No roentgen treatment has been given since.

DR. C. R. HALLORAN: The patient was given twelve roentgen treatments, and I am inclined to believe that they cured the acne rosacea. There is nothing new in the use of sulphur for acne. Dr. Ayres is always pleased when he finds Demodex folliculorum. There is a great difference of opinion as to whether this mite is the cause of acne rosacea. Most authorities, I believe, do not consider it as the cause.

GRANULOMA ANNULARE (?). Presented by DR. NELSON P. ANDERSON.

This schoolgirl, aged 12, was first seen on June 22, 1933, complaining of an eruption in the popliteal fossae which had been present for six or eight months. The eruption started as a small lump and gradually increased in size; more or less clearing had occurred in the center.

The patient's past history was unimportant, and although she was underweight for her age, there was no history of tuberculosis in the family except in a second cousin.

On examination, each popliteal fossa presented an irregular lesion the size of a hand with a firm, red, raised, circinate border and a clear center. There was a similar lesion the size of a silver quarter on the left leg below the knee.

Including a treatment today, the patient has received 2 skin units of roentgen radiation given in doses of one-half skin unit about a month apart. An extract of malt with cod liver oil has also been prescribed.

DISCUSSION

DR. MOSES SCHOLTZ: It is hard to conceive of this eruption as granuloma annulare. The lesions are flat and spread out. There is little infiltration. I am inclined to consider it parapsoriasis en plaques. I was struck by the bandlike shape of the lesions.

DR. W. H. GOECKERMAN: I believe that the eruption is granuloma annulare. There is too much infiltration for parapsoriasis, and the borders are too sharply defined. It is not ordinary granuloma annulare, but I cannot classify it any better.

DR. C. R. HALLORAN: Will Dr. Anderson make a biopsy and report on the case at the next meeting?

DR. NELSON P. ANDERSON: If Dr. Scholtz had seen this patient before treatment was given, I am sure there would be no doubt in his mind about the infiltration of the borders. The lesions now present only slight elevation and infiltration, but considerable change has taken place since the last roentgen treatment. The patient has had four doses of one-half skin unit at intervals of about a month.

CHRONIC ULCERATION OF THE SOLES (BOWEN'S DISEASE?): MULTIPLE BENIGN SUPERFICIAL EPITHELIOMAS; ARSENICAL KERATOSES (PALMS, SOLES, TRUNK). Presented by DR. SAMUEL AYRES, JR.

E. A., a man over 60 years old, has had trouble with his feet for nineteen years. It began with what appeared to be a callus on the outer side of the right foot. This later formed an ulcer, which was excised. The lesion did not heal, and roentgen radiation was applied. The lesion responded but broke down again. After the application of radium, it remained healed for about ten years. An ulcer then developed on the left heel which was removed surgically but required about one and one-half years to granulate; it remained well for three or four years. One

year ago a callus developed on the right heel. "Corn medicine" was applied, but soon an ulcer appeared. This was excised and finally healed, but after a chiropodist excised some scar tissue the area became ulcerated and has remained so.

When the patient was a student in college he took a large bottle of solution of potassium arsenite for eczema. This caused considerable swelling of the hands and fingers. So far as he knows, he has not been exposed to arsenic since.

There are numerous warty keratoses on the palms, varying in size from that of a pinhead to that of a split pea, and the skin of the palms is very dry. Many dry keratoses similar in size and appearance to those on the palms are present on the body, some gray to brownish ones being scattered over the arms, trunk and legs. There are eight or ten plaquelike areas on the trunk which have a dry, erythematosquamous, slightly atrophic surface and range in size from that of a pea to that of a half-dollar. Some of these lesions show pearly borders, and one on the upper part of the back has a well marked, doughnut-shaped pearly border with a depressed, crusted center.

Scattered over the soles are a number of keratoses similar to those on the palms but larger. On the plantar aspect of the left heel is an oval ulceration the size of a silver dollar; a portion of it has healed, but there is a deep raw portion the size of a dime. There are three smaller ulcerations. Telangiectasia may be noted.

A twenty-four hour specimen of urine obtained after a preliminary injection of sodium thiosulphate when tested by the Gutzeit method revealed 0.0027 mg. of arsenic per hundred cubic centimeters of urine, or 0.048 mg. per hundred grains of solid substance.

The finding of this small amount of arsenic does not prove the arsenical origin of these lesions, but this finding together with the history of taking considerable arsenic which provoked toxic manifestations at the time, the multiplicity of the epitheliomas, the characteristic arsenical keratoses of the palms and soles and the ulcerative lesions of the feet suggests arsenic as an underlying cause. This symptom complex is another example of the cases which Anderson recently reported in which multiple, superficial epitheliomas, arsenical keratoses, a history of exposure to arsenic, the finding of arsenic in the urine and, in one case, Bowen's so-called precancerous dermatosis all occurred in the same person.

DISCUSSION

DR. SAMUEL AYRES, JR.: This patient consulted me primarily on account of lesions on his feet. He could hardly walk. At first I thought that he probably had a chronic roentgen dermatitis; but apparently ulceration developed before roentgen radiation was used, and while his soles show a certain amount of telangiectasia, I think that the primary factor is keratosis which has undergone malignant degeneration. It is interesting to see apparently malignant degeneration of lesions on the feet and typical arsenical keratoses of the palms, soles and trunk together with multiple epitheliomas on the body and arsenic in the urine, even though in small amount. These findings certainly suggest arsenic as the cause of the entire symptom complex.

DR. KENDAL FROST: The thing that bothers me is why such late arsenical changes in the skin occur. All dermatologists recognize them. However, many people during most of their lives take more arsenic than the patients who present this reaction and show no changes. There is a determinable amount of arsenic in the Los Angeles city water, and there are other sources besides medication. There must be some factor in addition to arsenic to cause this picture.

DR. MOSES SCHOLTZ: I think that this case demonstrates well the power of arsenic to produce epithelioma. There are punctate keratoses, Bowen's superficial epitheliomas and finally crater-like ulcers. It is easy to conceive that arsenic stimulates the growth of epithelial tissue.

DR. L. F. X. WILHELM: This case is interesting. I have a patient at the present time who shows two of these manifestations. He has superficial epi-

theliomas on the body and definite arsenical keratoses on the palms but does not have the third symptom here presented. He took solution of potassium arsenite for several years for epilepsy.

DR. SAMUEL AYRES, JR.: I am giving the patient sodium thiosulphate, not to cure the lesions but to prevent their further development. The epitheliomas have been treated with radium and carbon dioxide snow. The ulcers on the feet are responding remarkably to ultraviolet irradiation.

PAPULONECROTIC TUBERCULID. Presented by DR. STANLEY O. CHAMBERS.

This American Jew, aged 41, for several years has had recurrent attacks of a papular eruption involving the ankles, lower parts of the legs, forearms, elbows and ears. There is a history of pulmonary tuberculosis for ten or twelve years, but at present the process is arrested. The Wassermann reaction of the blood was negative, and examination of the sputum for tubercle bacilli revealed none.

There are a few pitted scars over the extensor surfaces of the elbows, knees and ankles, and the ears appear moth-eaten. Distributed over the lower parts of the legs and the forearms are deep-seated necrotic papules. The picture is compatible with a diagnosis of papulonecrotic tuberculid. I call attention to the association of necrotic papules, scarring on the elbows and knees, a moth-eaten appearance of the ears and pulmonary tuberculosis.

DR. SAMUEL AYRES, JR.: I recently saw a case of papulonecrotic tuberculid in a girl of 18 with lesions on the elbows and some on the legs. She was given gold and sodium thiosulphate, and the condition entirely cleared.

DR. STANLEY O. CHAMBERS: This patient was also given gold and sodium thiosulphate and is now receiving neoarsphenamine. He failed to respond to gold, but the condition has improved following the administration of neoarsphenamine.

DR. W. H. GOECKERMAN: I have seen a number of cases of this type in which the patients were treated with both neoarsphenamine and gold preparations. I have not made up my mind as to which method is superior. I have seen each fail and each succeed.

DR. KENDAL FROST: I have under observation a young woman with tuberculids of the papulonecrotic type who has been treated with neoarsphenamine, gold and sodium thiosulphate and bismuth. No improvement has followed any of these agents. The association of open pulmonary tuberculosis with the tuberculids in the case presented tonight is interesting. I have asked some of the men working in the field of tuberculosis about the incidence of tuberculids in their patients, and they tell me that the combination is very infrequent.

DR. MOSES SCHOLTZ: I read in the French literature that in several cases of tuberculids injections of gold preparations had a tendency to provoke tuberculosis of the acute type. For that reason, it seems preferable in this type of case, to try first small doses of arsenic rather than a gold compound.

PHILADELPHIA DERMATOLOGICAL SOCIETY

R. L. GILMAN, M.D., *Secretary*

Oct. 20, 1933

J. P. GUEQUIERRE, M.D., *Presiding*

LEUKODERMA, TREATED WITH GOLD AND SODIUM THIOSULPHATE. Presented by DR. C. S. WRIGHT.

H. A., a white man, aged 38, in December, 1932, began to have a dry, scaly, eczematoid eruption on each side of the face. He was given five roentgen treatments in Scranton, Pa. Scales from the face were examined by a commercial lab-

oratory, and it was claimed that mycelia and spores were found. In May, 1933, he consulted Dr. Schamberg, at which time he presented an extensive crusting of the face and neck. The patient did not seek a physician again until August, 1933, at which time the eruption had entirely healed, and he presented an extensive leukoderma of the face and neck, with patches of total depigmentation surrounded by what appeared to be hyperpigmentation. He was given six injections of gold and sodium thiosulphate and in two months the patches of depigmentation on the face disappeared and those on the neck greatly improved although there was still some lack of pigment. He is presented to show the therapeutic result following the use of gold and sodium thiosulphate.

DISCUSSION

DR. A. STRAUSS: I did not see the patient before treatment, but my opinion is that treatment is of very little value in vitiligo. Those cases that clear up under treatment would clear up spontaneously. I have tried all the new treatments that have been in vogue and none of them has seemed to work. In a case of vitiligo at Mount Sinai Hospital, yellow atrophy of the liver developed, with death, following the use of a gold preparation.

DR. R. L. GILMAN: I think that the patient shows a very good result. As Dr. Strauss said, he was not seen by the members before treatment, but it seems that the condition has responded to something, probably to the gold compound. I should like to ask Dr. Wright if there was any intermediary dermatitis of the patches as a result of treatment.

DR. C. S. WRIGHT: This man presented dermatitis of the face caused by some local application; after that he received the gold compound. No eruption developed from one administration of the gold preparation. There is one point that I might make here. I usually dissolve the ampule of 25 mg. of gold and sodium thiosulphate in 10 cc. of a solution of sodium thiosulphate, believing that this lessens the tendency to dermatitis. It is purely empirical, but I have seen no resultant dermatitis when the gold was dissolved in this way. The main point in this case is that the patient presented an extensive leukoderma. Dr. Cobane saw him and can vouch for the fact that the entire face was much worse than the neck is now. This is only the second time that I have used a gold compound in treating vitiligo, and I am not particularly familiar with its value.

DR. F. D. WEIDMAN: I should like to ask if this case was regarded as one of true vitiligo or as one of symptomatic leukoderma, i. e., preceding dermatosis on which the vitiligo was imposed.

DR. C. S. WRIGHT: When I first saw him he had marked dermatitis. I thought it the result of treatment.

DR. J. M. SCHILDKRAUT: I have used a gold compound with local applications of bergamot and alcohol followed by irradiation with ultraviolet rays in a case that turned out favorably. I have used bergamot alone and have had no results.

DR. S. S. GREENBAUM: I have treated a number of patients with vitiligo by this method with disappointing results, but in view of the fact that two or three patients have now been reported as benefited by it, there seems to be indicated a different etiology in some cases of vitiligo. I have some patients under treatment now; the leukodermic skin has been getting red, and that is about all thus far. I have not been able to induce a return of any pigment with the use of a gold preparation, ultravolet rays and oil of bergamot. May I add, apropos of the treatment of vitiligo, that two other types of therapy have been recently proposed: the intravenous use of acriflavine hydrochloride and the cutaneous application of eosin in the dilution of 1: 5,000, plus irradiation with ultravolet rays in either case.

DR. C. S. WRIGHT: I thought that the treatment of vitiligo with gold preparations should be fully discussed in order to decide on its value before treating all cases of vitiligo with gold compounds. If dermatitis is apt to develop, or an accident such as yellow atrophy is possible, the medical profession will incur trouble from indiscriminate attempts to cure vitiligo with gold preparations.

A Case for Diagnosis; Kaposi's Sarcoma (?). Presented by Dr. C. S. Wright.

D. W., a Scotch seaman, aged 30, presents an extensive purplish eruption of the lower third of each leg and the ankles with papules the size of a pinhead and a few deep-seated nodules, rather painful to the touch, of nine months' duration. This patient was seen for the first time only twenty-four hours ago, and a biopsy was recommended. Clinically the condition suggests Kaposi's hemorrhagic sarcoma. The patient is an oiler and on his feet a great deal.

DISCUSSION

Dr. D. M. Sidlick: The condition resembles progressive pigmentary dermatosis, although that disease does not present induration of the type observed in this patient, particularly in the left leg. There should be cayenne pepper spots. In this particular case, considerable pressure is necessary to cause fading and even that does not leave a residual discoloration.

As regards Kaposi's hemorrhagic sarcoma, the cases I have seen presented deep infiltration of the tissues, and there was not the symmetry of distribution seen in this case. There is a possibility that this is a dermatitis of hemorrhagic eczema caused by varicosities. If the patient is obliged to stand all day long that may contribute.

Dr. F. D. Weidman: I think that Dr. Wright's point is well taken. On the upper parts of the legs is a soft, brownish pigmentation—a good cayenne pepper effect—but down below there is verrucous infiltration, which, as far as I know, is incompatible with progressive pigmentary dermatosis. It may be that this is a case in the period of transition, and therefore valuable as showing something in common in the pathologic processes of the two conditions. There is a large factor of hemosiderin pigmentation here; this obtains both in Kaposi's disease and in progressive pigmentary dermatosis. However, there are only a few cases of Kaposi's sarcoma that are not Galician in origin; this patient is not a Jew. One of the latest lines of inquiry Dr. Schamberg was following in progressive pigmentary dermatosis was that of the cholesterol in the blood. That might also be investigated.

Dr. S. S. Greenbaum: What has been found in other cases with regard to the cholesterol content of the blood? Dr. Schamberg reported two cases as showing high cholesterol.

Dr. C. S. Wright: There hasn't been a case presented here since then.

Dr. J. M. Schildkraut: I had a case with the blood showing a high cholesterol content.

Dr. Rose Hirschler: I remember seeing a case of progressive pigmentary dermatosis many years ago, in which the spots resembling cayenne pepper were very marked, and the lower part of the leg showed pigmentation with scant infiltration. This man has such deep infiltration around the lesions of the one leg, and there is so much purple color, that I should be afraid of something insidious in the process, slow and inclined toward malignancy. He has had it quite a long time.

Acute Lupus Erythematosus. Presented by Dr. C. S. Wright and Dr. R. Friedman.

J. M., a white woman, aged 36, stated that following the extraction of a tooth in December, 1932, her face swelled and was covered with an inflammatory, oozing and crusted eruption, which spread to the scalp and subsequently involved the arms, hands, chest and abdomen. On May 17, 1933, she was admitted to the ward for the treatment of cutaneous diseases in one of the local hospitals, where she remained until June 6, when, mental symptoms having developed, she was transferred to the psychopathic ward. She was discharged from the hospital

on June 22, the cutaneous as well as the mental condition having been considerably relieved. The diagnosis on admission was toxic erythema multiforme (?), acute eczema (?), Duhring's disease (?). The diagnosis on discharge from the hospital was residual dermatitis multiforme and toxic psychosis. On the day of admission to the hospital, the temperature reached 104 F. at 5 p. m. The temperature gradually subsided and became approximately normal about May 26, and remained virtually normal until she was discharged. The Wassermann reactions of the blood and spinal fluid were negative.

The patient was first seen in the Temple University Dispensary on Sept. 29, 1933. According to the history, there was a recurrence of the inflammatory eruption of the face on September 20. On examination, the face presented a reddish-purple, patchy and coalescent, dry, somewhat scaly maculopapular eruption involving virtually all of the face and forehead, with the exception of the circumoral and periorbital regions. Both ears were also involved, as were the outer aspects of both arms and the upper middle part of the chest. Some oozing and crusting were present on the ears, arms and chest. Small maculopapular lesions were also present on the forearms, hands and upper part of the back. The back presented brownish pigmented macules of various sizes, evidently the healed remains of the first attack. There was virtually no involvement of the lower extremities. The mucosa of the roof of the mouth about the junction of the middle and soft palates presented a group of papular lesions, many of which had undergone superficial ulceration. Since admission to the Temple University Hospital on October 4, the patient has had an irregular febrile temperature, sometimes reaching 102 F. A Mantoux test was done on October 11. Three hours later, the patient had a severe outbreak of urticaria, followed by a chill and a rise in temperature. A marked local reaction took place. Clinical examination of the chest showed signs suggestive of tuberculosis.

DISCUSSION

DR. E. F. CORSON: I agree with the diagnosis. Dr. Cohen, who attended the patient first, said that the appearance was quite different in the beginning. I recently saw a case in which the eruption began in a fashion that precluded the diagnosis of disseminated lupus but later flattened out and took on many of the aspects of the eruption in the case presented here. All one could see in the beginning was an erythema solare coming on after severe exposure to the sun, but in due course the scaling and margination, telangiectasia, sebaceous plugs, etc., put in their appearance.

DR. B. KAHN: This patient was admitted to the Philadelphia General Hospital last April. The whole body was involved in vesicular, bullous lesions, with hardly a spot not covered. It was difficult to keep her in bed; the pillows and mattresses became saturated with blood that oozed from every part of her body. My associates and I could not understand her case. There was no history. We thought that perhaps we were dealing with an acute chemical dermatitis. We covered her completely with petrolatum-treated gauze, and after keeping her that way for about a week or two the back practically cleared up and she left the hospital shortly afterward. I was surprised to see her with a diagnosis of lupus erythematosus. When we saw her the condition did not look anything like that.

DR. S. S. GREENBAUM: What did the blood count show?

DR. R. FRIEDMAN: The blood picture is in keeping with the diagnosis of acute lupus erythematosus. On October 4 it showed leukopenia, with a white cell count of 3,000; on October 6, one of 3,700.

DR. S. S. GREENBAUM: Dermatologists have been lax in examining the blood pictures in acute lupus erythematosus, and there is a question whether leukopenia is to be universally accepted as indicative of acute lupus erythematosus. The cases do not all show leukopenia; in the last five at the Philadelphia General Hospital the white cell counts were within the normal range. A case resulting in death that I saw there this summer showed a white cell count of 6,300. The pathol-

ogist made a careful differential count of the white cells and prognosticated that death would take place within ninety-six hours. The patient died within forty-eight hours. All cases of acute lupus erythematosus ought to be carefully examined from the standpoint of the white cells, immature forms and Schilling's indexes because of their prognostic value.

DR. F. D. WEIDMAN: Did this patient always have that unnatural lurid pink color that makes one think of an eruption from a drug?

DR. R. FRIEDMAN: Acute lupus erythematosus is usually associated with arthritic symptoms. There was an article in the *British Journal of Dermatology* concerning seven cases of acute lupus erythematosus, five of which were complicated by arthritis. I observed a case about a year ago, for which about seven white cell counts were made, all of which showed 4,000 or less. The patient had marked pains in the joints, and died in the twelfth week of the disease.

LEUKOPLAKIA OR LICHEN PLANUS CONFINED TO THE MOUTH (?). Presented by DR. F. D. WEIDMAN.

J. S., a man, 59 years old, a cabinet-maker, presents a pearly-white reticulation on the mucosa of both buccal surfaces, suggesting lichen planus. However, the tissue comprising the reticulation is denser and less macerated than in lichen planus. I believe the condition to be leukoplakia with a peculiar configuration. There was at one time a patch of superficial scaliness on the left forearm, but it could not be identified as lichen planus. There are no other dermatologic changes elsewhere on the body.

The condition began as a nodule in the mouth in May, 1932. This was 2 cm. long and hard, and was located on the left alveolar margin extending into the buccal mucosa. It bled easily when manipulated. It was excised and reported as spinous cell carcinoma, grade 2. On Oct. 13, 1932, the mass had disappeared. The patient had been given treatment with radium from May, 1932 to January, 1933, a total of about 30,000 mg. hours.

DISCUSSION

DR. E. F. CORSON: I think that the condition is leukoplakia.

DR. S. S. GREENBAUM: I have never seen leukoplakia produce reticulation of this sort. The earliest disturbance in leukoplakia is a smoothing out and reddening of the mucous membrane of either the tongue or the buccal mucosa, followed by keratinization or graying clinically. But this reticulation, with at least half a dozen small white papules the size of a pinpoint (hardly papules, they are so minute), seems to fit in with lichen planus limited to the mucous membrane. There is no way to prove it except, perhaps, histologically.

THREE CASES OF GRANULOMA INGUINALE TREATED WITH FUADIN. Presented by DR. J. H. COBANE for DR. S. S. GREENBAUM.

W. H., a Negress, aged 37, had, when examined on Sept. 20, 1933, a superficial, ulcerating, spreading, vegetative, red granuloma. At the present time the growth is practically healed after eight injections of fuadin. The pain and tenderness disappeared after four injections. The condition is of seven years' duration, and the patient received from fifty to seventy-five injections of antimony and potassium tartrate with benefit.

L. E., a Negress, aged 31, was given nine injections of fuadin in the treatment of an irregular, superficially eroded, red, painful granuloma of the left labium majus. Pain disappeared after the third injection.

B. B., a Negress, aged 25, has received seven injections of fuadin. Much previous treatment with antimony and potassium tartrate was ineffective.

DISCUSSION

DR. S. S. GREENBAUM: These cases were presented to show the effects of the new antimony compound, fuadin, on inguinal granuloma. Not only has it been perfectly tolerated by the patients treated recently, but it is painless and is particularly efficacious. It has been remarkable to see what it has done to these cases of granuloma inguinale. The first thing to disappear with the first injection is the pain. Only ten injections are needed and usually by the tenth the entire lesion, no matter how large it is, is cicatrized. One girl, B. B., came to the clinic for years. She was an irregular patient; heretofore, treatment with antimony required daily intravenous administration, and patients tired of coming. At one time I did a vulvectomy on this patient to relieve an elephantiasic vulva. The condition cleared up wonderfully under the new treatment. I have also used this compound in other diseases of the skin, particularly in dermatitis herpetiformis, and in one case shown here tonight the result has been surprising. I intend to pursue the study of the effects of this particular type of antimony and other compounds in other diseases of the skin and in syphilis.

I have used fuadin in treating lymphogranulomatosis inguinalis. In acute forms of the condition it does not appear to be of much value. In chronic forms it appears to be of distinct value, and in one case of five years' duration marked improvement took place. The induration and scarring that go with chronic forms of lymphogranulomatosis inguinalis remained, but the odor, the pain and the discharge were so favorably influenced that I believe it to be of definite value in treating these chronic forms.

DERMATITIS HERPETIFORMIS. Presented by DR. COBANE for DR. S. S. GREENBAUM.

E. W., a woman, aged about 30, was presented to the society last year with widespread severe dermatitis herpetiformis, made worse for diagnostic purposes by the administration of iodides. She is now presented to show that the condition has entirely cleared up following the use of fuadin. The itching disappeared after the first injection, and the lesions were nearly gone after three injections given over a period of nine days.

NECROTIC ULCERS OF UNKNOWN ETIOLOGY. Presented by DR. J. H. COBANE for DR. S. S. GREENBAUM.

P. W., a man, aged 43, entered the Graduate Hospital of the University of Pennsylvania in August, 1927, complaining of numerous furuncular lesions on the back. The results of the Kolmer and Kahn tests were positive. He was given two injections of potassium bismuth tartrate, and then disappeared from the clinic for six years. He reappeared in July, 1933, showing extensive necrotic ulceration below each axilla and many keloids on the back. The Wassermann reaction was negative.

The ulceration on the right flank healed completely after thirteen injections of a water-soluble bismuth preparation, seven injections of an oil-soluble bismuth preparation and seven injections of neoarsphenamine. The lesion on the left flank did not respond to this therapy. A Kahn test of the blood on Aug. 7, 1933, showed a mild serologic relapse; the Kolmer test was negative. Examination of the spinal fluid yielded negative results.

Biopsy specimens from the lesions on the right and left flanks are shown.

DISCUSSION

DR. S. S. GREENBAUM: This is a very interesting case. I have seen, I think, two or three like it. It can only be grouped, if it is to be classified, with syphilis that is resistant to arsenic and bismuth, or as an "ulcus molle (non-chancroidal)" due to some other organism than the streptobacillus, perhaps to the

diphtheroid or pyococcus. In four patients in whom I have seen this particular type of ulceration, cure was obtained only by destroying the lesions. Autoinoculation was done in this case, with negative results.

DR. J. H. COBANE: The ulceration seems to have increased since last summer. There seems to be ulceration under the epiderm.

A CASE FOR DIAGNOSIS; VERRUCOUS DERMATOSIS OF THE LEGS. Presented by DR. F. D. WEIDMAN.

L. W., aged 50, a hospital orderly, a potential subject for diabetes whose condition, however, is easily controlled by diet, had as his first complaint a carbuncle and a nodule on the back of the neck in 1923. The lesion was treated by fulguration and did not recur. In 1931 a similar nodule back of the ear was treated by fulguration. On July 1, 1932, he reported a nodule the size of a bean on the back of the neck, which was treated by electrodesiccation, followed by irradiation with roentgen rays. The histologic report on the second specimen was that it was squamous cell cancer; that on the third was that it roused a suspicion of squamous cell cancer. On Aug. 8, 1932, a small nodule made its appearance near the last one; it was similarly treated. It was reported on histologically as a "hyperkeratinized wart with suspicious malignant changes." Recurrences took place at the margins of the latter two lesions, which, however, eventually yielded to long continued treatment by irradiation.

The lesions on the leg began to appear about Jan. 1, 1933. They were furunculoid and were treated as such by Dr. Klauder. On March 17, nodules developed on one elbow and on both wrists which were epitheliomatous clinically. Radiation therapy had no effect on any of these. Histologically there was no support for the diagnosis of tuberculosis or sporotrichosis; the lesions were massive acanthomas.

Biopsy specimens taken in May from the ankle and sole showed no cancer, tuberculosis or sporotrichosis; only a pseudo-epitheliomatous hyperplasia and keratosis. Inoculation of guinea-pigs gave negative results. Staphylococcus aureus, Staphylococcus albus and diphtheroids were cultured. Iodides were given intravenously three times in May, with improvement in the lesions at first, but not later.

DISCUSSION

DR. F. D. WEIDMAN: Essentially, the growth on the leg is an overgrowth of the epidermal structures. The man also has plantar warts. The lesions on the leg regress spontaneously. I produced one lesion experimentally by the injection of a filamentous fungus isolated from a piece of tissue, using physiologic solution of sodium chloride as the control injection. I plan to repeat that test. I think that it is some peculiar kind of verruca and that, if located on the sole, the lesions would have the characteristics of plantar warts. I am showing the case largely for comments on the diagnosis.

DR. J. M. SCHILDKRAUT: Those lesions impressed me as a giant type of molluscum contagiosum.

DR. S. S. GREENBAUM: One or two of the lesions had definite central orifices resembling those which one would see in molluscum contagiosum, and I believe that in one of the sections I saw distinct evidence of molluscum contagiosum.

DR. D. M. SIDLICK: Is is possible for molluscum contagiosum to attain this size?

DR. S. S. GREENBAUM: I believe that giant types have been described.

DR. E. F. CORSON: The lesions with the built up conical structure somewhat remotely resemble keratoderma haemorrhagica. I do not know about the histologic structure of hemorrhagic keratoderma, and I did not see the slide, but the growths on the sole didn't look exactly like plantar warts to me. I could make out no definite warty structure. I did not see the type alluded to by Dr. Greenbaum resembling molluscum contagiosum, but there was a conical squamous top to some

that looked like a gonococcic infection of the skin. According to the history, the patient had that disease in 1926 for the first time.

DR. D. M. SIDLICK: It is my impression that in keratosis haemorrhagica there is a urethral discharge. I did not question the patient as to whether he had any swollen joints or a urethral discharge. I did not see all the lesions, but those that I saw did not impress me as being of the nature of keratosis haemorrhagica.

A CASE FOR DIAGNOSIS; HERPES IRIS OF UNUSUAL DURATION (?). Presented by DR. F. D. WEIDMAN.

H. C., aged 43, a junk dealer, in July, 1933, noticed a blister on the foot from which blisters spread to the entire body in three days. There were red patches and big blisters, and the condition was diagnosed as erythema iris. Several weeks later the bullae gradually disappeared. Pus was evacuated from nodes in the axillae. Nine days later there was a recurrence of blebs, but not so much systemic reaction. There was no history of taking drugs. The blood culture gave negative results.

DISCUSSION

DR. F. D. WEIDMAN: When I first saw the patient a few blebs were still present. However, the persistent brown pigmentation and infiltration of some of the lesions made me wonder whether it could have been bullous lichen planus. The condition began over three months ago, which seems a long duration for ordinary herpes iris. I can't see any lesions definitely resembling lichen planus at present. It would have to be in the hypertrophic stage.

DR. S. S. GREENBAUM: When this man was admitted there was a fairly widespread vesiculobullous eruption, with a herpes iris type of lesion particularly marked on the forearms. It was diagnosed as pemphigus by those who admitted him, and I made a diagnosis of erythema multiforme of the bullous type. There are no lesions of lichen planus on the body. The lesions on disappearing, as they did once or twice during the time that the patient was under observation, were replaced by pigmentation and discoid papules which tended to disappear slowly. A culture was made of the blebs and a streptococcus found. At no time was the temperature elevated. The patient was given iodine, and the condition began to clear up. If this is a bullous type of lichen planus it occurs in a person who does not have lesions of lichen planus and who has not had any during the time that I have seen him. Of the several patients with blebs in the presence of an eruption of lichen planus that I have seen, all have been previously treated with arsenic; and when bullous lesions develop in the course of lichen planus heavy metal therapy as the cause should be excluded.

DR. A. STRAUSS: I have at present a patient with generalized lichen planus whom I have treated since the beginning of the disease, and who has never had any arsenic. She has had nothing but bismuth. Recently, toward the end of the disease, a terrific bullous outbreak occurred, with blebs as big as hen's eggs, especially on the lower extremities.

DR. S. S. GREENBAUM: Can you exclude eruption due to treatment with bismuth?

DR. J. P. GUEQUIRRE: Cases of lichen planus in which blebs developed have been reported from England as having occurred in persons who had received no arsenic.

A CASE FOR DIAGNOSIS. Presented by DR. J. H. COBANE for DR. S. S. GREENBAUM.

R. M., a woman, aged 40, was presented at the meeting of the Atlantic Dermatological Conference in Philadelphia in 1932. She is presented again because of the somewhat changed picture, showing on the flexor surface of the left forearm

a patch eruption that consists of individual pink, infiltrated, slightly scaly, arc-shaped, papular lesions, confluent in one area to form a gyrate or serpiginous configuration and in another area to form a more or less diffuse patch. On the ulnar side of the dorsum of the left forearm is a similar patch with little infiltration and some scaling. On the ulnar side of the right forearm are the remains of a lesion which the patient says was similar to that described. At the present time it shows pigmentation and atrophy. There is a history of much roentgen therapy to those three areas.

The Wassermann reaction of the blood on Sept. 22, 1933, was negative. The biopsy of September 29 was reported as follows: Under low power magnification the cutaneous disturbances seem to be limited entirely to the epidermis and the derm. The horny layer is thickened; at various points the horny cells have retained their nuclei, but the parakeratosis is not present throughout; at certain points between the horny lamina there are large collections of cells with darkly stained nuclei which under a high power lens appear to be lymphocytes and polymorphonuclears. These collections are much larger than those generally seen in psoriasis. The prickle cell layer is thickened and more than moderately infiltrated by cells extending to the lower limits of the derm; clearly defined papillary prolongation and interpapillary pegs are only occasionally discernible and there are many intercellular spaces of various sizes (edema?) in the prickle cell layer. Under high power magnification the infiltrating cells appear to be mainly of white cell origin. The histologic picture suggests an inflammatory condition, but one that does not fit in with any particular cutaneous entity.

The blood count was: red cells, 4,180,000; hemoglobin, 72 per cent; leukocytes, 10,200; polymorphonuclears, 65 per cent; eosinophils, 2 per cent; lymphocytes, 30 per cent, and transitionals, 3 per cent.

DISCUSSION

DR. E. F. CORSON: I had this patient under observation. She was presented at the Atlantic Dermatological Conference last November. The biopsy and the findings were not definitely indicative of any diagnosis. Tertiary syphilis was first thought of, but the Wassermann reaction was always negative. The possibility of beginning mycosis fungoides was considered; there was some curious serpiginous granulomatous structure which suggested it. Some one thought that the sections resembled granuloma annulare. Even sarcoid was thought of. Several of the lesions cleared up promptly under roentgen treatment, some did not and others recurred.

DR. C. S. WRIGHT: This patient was seen by Dr. Schamberg, who made a positive diagnosis of psoriasis.

DR. F. D. WEIDMAN: There are definite areas of atrophy here which are not found in psoriasis; some, according to the history, are of months' duration. They are not scars; the only scar to be found is at the site from which the specimen was taken for the previous biopsy. In other areas the skin is soft and velvety. There is atrophy rather than scar formation, and that points to one of the superficial processes like granuloma annulare or something of that nature. I venture to suggest porokeratosis of Mibelli, although the picture is not typical.

DR. E. F. CORSON: I suggest sarcoid or tuberculosis of the skin. Dr. Wise thought the lesions were tuberculous.

DR. S. S. GREENBAUM: Of course, the original clinical picture on the woman's arm has been altered as a result of previous treatment. She has had some roentgen therapy. But if you look closely at the infiltration in that lesion you will see that it is not psoriatic. I should be more inclined to think of a peculiar type of granuloma annulare.

NEW YORK DERMATOLOGICAL SOCIETY

RAY H. RULISON, M.D., *Secretary*

Regular Meeting, Oct. 24, 1933

EDWARD R. MALONEY, M.D., *President*

ARGYROSIS (?) OF THE NAIL BEDS. Presented by DR. FRED WISE.

P. L. S., aged 39, married, mother of three children, is presented because of a bluish discoloration of the proximal portions of the nail beds on the fingers. The nails themselves (as also the toe-nails) are normal in appearance. Physical examination reveals no other abnormalities. The proximal portions of the nail beds on all the fingers show a light blue discoloration extending from the cuticle to half-way up the nail, the distal edge of the discoloration merging gradually with the normal tint of the nail bed. Pressure on the nails causes nearly complete vanishing of the blue tint. The patient states that a bluish tint also occurs on the face, especially about the nose and mouth, and that it becomes more pronounced before and during the menses. The discoloration has been present for three years. The patient used a solution of mild silver protein in the nostrils with more or less regularity from 1927 to 1932, and she first noticed the bluish tint under the nails in 1930. The subungual tint is not the slate-gray seen in argyria. A capillaroscopic examination of the nails will be made on a future visit.

DISCUSSION

DR. WALTER J. HIGHMAN: This case interests me because last summer a report appeared, published by Sherwood Wright in *The Journal of the American Medical Association,* on the necessity for differentiation among the various causes of discoloration of the nails at the site at which Dr. Wise's patient shows it. Wright pointed out that in instances which cannot be explained otherwise frequently the initial stage of argyria causes the phenomenon. When this can be proved it is an indication to interrupt the use of silver preparations. When I saw this patient it impressed me that very likely she exhibited a condition of the group mentioned by Wright. In the history presented by Dr. Wise it was stated that for a period of five years ending with 1932, I believe, the patient had used a solution of mild silver protein daily for sinusitis. Incidentally, on the forehead and other areas of the face not covered by cosmetics, as well as on the dorsum of the hand, a slight ivory blue tint of the skin is visible. Thus this is more than an incipient case of argyria; it is probably a fully developed case, not likely to advance, since the use of the drug has been interrupted. From the standpoint of general medicine this is one of the most valuable cases that has been presented before the society for a long time. The article to which I have referred, in *The Journal of the American Medical Association* (**101**:439 [Aug. 5] 1933), is entitled: "The Clinical Value of Human Capillary Studies in Fever, Mental Deficiency, Nephritis, Vascular Diseases, Clubbed Fingers, Arthritis, Tobacco Smoking, and Argyria."

DR. FRED WISE: I accept Dr. Highman's interpretation. At the time this patient applied for treatment, she stated that she had used mild silver protein over a period of about five years, but we did not, I admit, consider the possibility that the condition was a discoloration caused by the preparation of silver, since pressure on the nail made the discoloration vanish. The patient also has a bluish discoloration of the face which can be discerned in a good light. This confirms Dr. Highman's interpretation.

SCLERODERMA OF THE LEFT UPPER EXTREMITY. Presented by DR. FRED WISE.

O. McF., aged 15, in good general health, is referred by Dr. C. G. Kerley for the treatment of two areas of scleroderma on the left upper extremity. One area, about 8 by 3 inches (about 21 by 8 cm.), extends from the point of the left

shoulder down the extensor surface of the arm, about half-way to the elbow. The surface is hard to the touch, and the skin appears to be bound down to the underlying fascia and musculature. There is a pronounced mottled leukoderma over this area. There is no pain. The other area affects the midportion of the radial surface of the forearm and is free from pigmentary changes. The skin between the two affected regions appears normal. The patient complains of dysmenorrhea, but is otherwise in good health. Dr. Kerley reports that the result of a test of the basal metabolism was normal and that the results of the physical examination were irrelevant.

This case is presented principally for suggestions as to therapy. I should like to know whether any one has had good results from the use of pancreatic extracts.

DISCUSSION

DR. GEORGE M. MACKEE: I have used "padutin" (a pancreatic preparation) in a number of cases and have seen no improvement.

DR. BINFORD THRONE: I have tried "padutin" in a number of cases and have not seen any effect.

DERMATITIS HERPETIFORMIS. Presented by DR. HOWARD FOX.

M. W., a man, aged 33, previously presented as having toxic erythema, was shown on April 25, 1933, with a profuse maculopapular eruption mostly on the trunk. There was no special grouping, and there was only slight objective evidence of scratching. It was also the first attack. Since that time the eruption has persisted with partial remissions under various forms of treatment. Recently the type has changed and now there are grouped papules which are severely excoriated.

DISCUSSION

DR. WALTER J. HIGHMAN: I should like to point out to Dr. Fox, if he is interested in suggestions as to therapeutics in relation to this case, that I have recently used injections of a preparation of the anterior lobe of the pituitary gland daily or two or three times a week in the treatment of dermatitis herpetiformis. It seems to control the process, and I think that it is worth trying.

ERYTHÈME ANNULAIRE CENTRIFUGE (DARIER). Presented by DR. FRED WISE.

P. C., a man, aged 53, born in Russia, came to the dermatologic clinic of the New York Post-Graduate Medical School and Hospital on Oct. 10, 1932, complaining of a sore throat, dizziness and headaches. He stated that he had had a penile lesion six years ago. The Wassermann reaction of the blood was negative on two occasions. The Wassermann reaction of the spinal fluid was negative, the globulin reaction was negative and the cell count was normal, but the colloidal gold reaction was positive for dementia paralytica. The patient received injections of neoarsphenamine and of a preparation of bismuth, and all the subjective symptoms disappeared. On April 7, 1933, he returned to the clinic with erythematous, scaly, well defined lesions on the groins. An examination for fungi revealed none. The lesions improved under application of Whitfield's ointment (50 per cent strength). The present eruptions on the thighs, abdomen, pubic region and left lateral surface of the chest and in the axillae have appeared during the past six months and at present seem to be quiescent, showing no appreciable progress. The eruption is seen in well defined, slightly elevated patches, varying in size from that of a goose egg to that of the palm of a hand, in color from salmon to light brown. The configuration varies, being annular, semiannular and gyrate, with central clearing and fading in some of the lesions. The outer edge of each lesion is smooth and slightly raised, while the inner one presents a moderate amount of scaling. There are a few similar lesions, ranging from the size of a dime to that of a cherry, scattered on the back and in the left axilla. The patient complains of occasional mild itching.

He is very accommodating. We shall obtain another specimen for biopsy and report the results at the next meeting.

NOTE.—The following report of the subsequent biopsy was given by Dr. D. L. Satenstein on Oct. 26, 1933: Microscopically this is a moderate exudative inflammatory process involving the upper cutis and the epidermis. There is a dilatation of the vessels of the middle and upper cutis, with a perivascular cellular infiltrate, in part limited to the perivascular lymphatic spaces and in part somewhat diffuse. There is considerable edema of the subepidermic zone extending up into the epidermis, with a somewhat regular dilatation of the lymphatic vessels. The epidermis is somewhat swollen owing to interstitial edema of the underlying structures, the granular layer being for the greater part well retained. No distinct parakeratosis is present; the basal cell layer, though disturbed, is well preserved. There are no changes like those seen in the early stages of mycosis fungoides.

DISCUSSION

DR. WALTER J. HIGHMAN: I think that this is erythema annulare centrifugum. I suppose that the inevitable question of mycosis will be raised. If it is mycosis, it is in so early a phase that it cannot be recognized clinically—only prophesied.

DR. J. FRANK FRASER: I agree with Dr. Highman. This may be a case of mycosis fungoides. The histologic picture does not show any evidence of that disease, but if more biopsies are made histologic evidence of mycosis fungoides may appear. One should not be satisfied with one biopsy.

DR. HOWARD FOX: It is not too early to suspect mycosis fungoides, though it may be too early to recognize it histologically. The eruption suggests mycosis fungoides on account of the circinate configuration and the uneven amount of infiltration in different parts of the lesions. On being questioned, this man said that the eruption did itch from time to time, and this changes the situation to a certain extent.

DR. BINFORD THRONE: I am inclined to agree with Dr. Wise. The presence or absence of pruritus in erythema annulare centrifugum is purely personal. Some patients complain of itch, and some do not. I think that you will find that stated in the reports of some of the cases. I can see nothing here but erythema annulare centrifugum.

UNILATERAL PSORIASIS (QUESTION OF NEVUS?). Presented by DR. E. F. TRAUB.

S. R., a stenographer, aged 23, born in the United States, states that an eruption appeared on the upper part of the left arm seven years ago and very gradually spread, following a linear arrangement, to involve the left arm, shoulder, axilla and side of the trunk. There are no lesions elsewhere on the body except on the scalp, where scaly patches are visible which suggest psoriasis rather than seborrheic dermatitis. The peculiar feature is the unilateral, linear arrangement suggestive of a nevus. The eruption has been very persistent; it has not disappeared since its onset seven years ago. There is a distinct suggestion of atrophy about the individual patches. The biopsy will be reported on later.

DISCUSSION

DR. HENRY H. WHITEHOUSE: I have never seen psoriasis localized in this way. I do not see why the condition cannot be called a nevus with resemblances to psoriasis. The pathologic picture will perhaps tell more.

DR. FRED WISE: Most of the articles and textbooks that deal with this type of lesion call it linear psoriasis, and the histologic appearance is that of psoriasis with no sign of nevus formation of any kind. A number of cases of linear psoriasis have been described, and in our clinic we have seen at least three in the past six or seven years. In some of the cases the condition cleared up with the use of chrysarobin salve but recurred soon after. Some of the men who presented cases

like this at the meetings of the section of dermatology of the New York Academy of Medicine regarded the condition as a nevoid psoriasis. I doubt very much whether one can interpret this as related in any way to a nevus; it has been called "nevus tardus."

DR. GEORGE M. MACKEE: I did not see the patient, but I am interested in this type of case. I should like to ask those of you who are particularly interested in histopathology whether or not it is possible from the histologic standpoint to differentiate between psoriasis and psoriasiform nevus. The mere fact that a lesion suggests psoriasis histologically does not prove that it is psoriasis or disprove that it is a nevus. Of course, if there is a typical histologic picture of psoriasis, as happens in some cases, in all probability the case is one of psoriasis. But when the histologic picture is not conclusive, how can one exclude a clinical nevus, and by clinical nevus I mean a lesion that does not contain nevus cells. I know of no way in which an unequivocal differentiation can be made except in occasional cases.

DR. JOSEPH J. ELLER: I consider this a nevus.

DR. WALTER J. HIGHMAN: I do not know what to say in answer to Dr. MacKee's question. At the beginning of his discussion he said that he would like an expression of opinion from the histologic standpoint, and at the end, quite correctly, he stated that none could be given and wanted an opinion from the clinical standpoint. I do not know just how to approach his request. If a nevus is described as an embryonal disturbance which in the retarded type manifests itself long after birth, I should say that, regardless of the histologic appearances, it is a nevus, whatever its gross appearance—psoriasiform, in this instance. If, on the other hand, the conception of a nevus is restricted to a lesion that shows nevus cells on histologic investigation, the problem becomes narrower. I used to take a much more arbitrary point of view. I admit that it would be difficult on the merits of the case to differentiate between what one is pleased to call a psoriasiform nevus and psoriasis with nevus-like distribution. I do not believe that this can be done either microscopically or clinically. My preference in this case would be to regard the lesion as the psoriasiform type of nevus.

DR. HOWARD FOX: There are on record cases of a lesion having the clinical appearance of psoriasis in linear form. If the lesion in this case showed undoubted psoriatic changes histologically I think that it should be called psoriasis. That disease is by no means always bilateral and at times there is only a single patch. The opinion is held by many that it may present a linear configuration.

DR. E. F. TRAUB: Doubtful cases of psoriasis with a nevoid arrangement have been frequently reported in the literature; in many of those cases, as in this one, there was a question whether psoriasis had not appeared in a rather unusual form which should be spoken of as linear psoriasis rather than connected in any way with a nevus. In this case, however, the presence of atrophy made me think that the lesion might possibly be a nevus resembling psoriasis rather than true psoriasis. The term "nevus tardus" has been mentioned, and I should like to say a word about that. I have recently looked carefully into the derivation of the word "nevus," and although a number of textbooks imply that it means "to be born with," it actually does not seem to mean more than "a blemish" or "a mark." As the vast majority of nevi are not present at birth but appear at varying times thereafter, the term "nevus tardus" means little and should not be added to the literature, because if all nevi that appear after birth were called "nevus tardus," the majority of nevi would bear this name.

MYCOSIS FUNGOIDES (?). Presented by DR. FRED WISE.

Mrs. R. S., aged 51, was recently under the observation of Dr. Pollitzer. Her disease of the skin began eleven years ago. She was previously presented by Dr. Abramowitz at the New York Academy of Medicine (ARCH. DERMAT. & SYPH. **20**:892 [Dec.] 1929). At that time she applied for treatment at the Post-

Graduate Medical School and Hospital. Her eruption was then of about seven years' duration; the eruption developed first on the arms and then became rapidly generalized. It was accompanied by severe itching. At the time of her initial visit to the clinic the eruption resembled a widespread neurodermite and there were no lesions resembling psoriasis, but the diagnosis of mycosis fungoides was considered. The histologic examination was reported in 1929 by Dr. Satenstein as follows: "There is a moderate irregular acanthosis, with a slight general perivascular cellular infiltration throughout the tissue. In one area involving the space of about twelve papillary bodies, the cellular infiltration is more marked and extends up to and into the epidermis. The epidermis in this region presents numerous vacuolated areas. A positive diagnosis cannot be made from this section, although the appearances are more in favor of chronic eczema than mycosis fungoides." The diagnosis of general exfoliating erythematous dermatitis was considered in 1929. At that time the majority of the members favored a clinical diagnosis of mycosis fungoides.

The eruption has become more extensive since 1929, now involving the skin of the entire body. There is an almost universal erythrodermia with hyperkeratosis, in the midst of which are innumerable elevated, scaly, erythematous and infiltrated plaques, affecting the face (even the eyelids), the scalp, and the upper part of the trunk as well as the extremities. On the chest, back, legs and arms there are in addition many red and violaceous nodular infiltrations resembling those of mycosis fungoides. Some of the patches closely simulate psoriasis.

DISCUSSION

DR. HENRY H. WHITEHOUSE: I think that pure psoriasis of this type and distribution is extremely rare and that this is just the type which later becomes mycosis fungoides. Cases have been reported in which a condition diagnosed as psoriasis and progressing as psoriasis for a long time developed later into mycosis fungoides. The question is whether in those cases the condition was not mycosis fungoides from the beginning. It is a thing difficult to demonstrate. I regard this case as of that type.

DR. PAUL E. BECHET: I agree with Dr. Whitehouse. There are undoubtedly cases of a frankly psoriasiform condition developing later into mycosis fungoides. I believe that Dr. Fox has reported several. Dr. Wise's case, I believe, is one of mycosis fungoides.

DR. E. F. TRAUB: Two years ago I presented before this society a patient whose condition had been diagnosed clinically as mycosis fungoides, and the diagnosis was substantiated subsequently by all the members of the society. This patient had had an eruption of over ten years' duration, diagnosed clinically by a number of the members of the society, before he had consulted me, as "straightforward psoriasis." Shortly before this patient's death, about a year after presentation, all the lesions that suggested psoriasis disappeared and in their stead numerous tumors developed, some located superficially and others deep in the subcutaneous tissue and muscles. When the patient was seen shortly before his death, a member of the society thought the case to be one of sarcoma because of the peculiar appearance of the tumors. The case, however, was one of mycosis fungoides from start to finish.

DR. J. FRANK FRASER: Dr. Whitehouse brought up the question whether this has been a case of mycosis fungoides from the beginning or a case of psoriasis which has become one of mycosis fungoides. There are cases on record in which psoriasis has given way to other conditions. For example, psoriasis may eventuate in exfoliative dermatitis. But regarding an exfoliative dermatitis which was originally psoriasis, Dr. Montgomery in a recent article brought out that one can determine histologically whether the exfoliative dermatitis was originally psoriasis, because histologically the features of psoriasis are retained. Now as to the case under discussion it is impossible to say whether originally it was a case of psoriasis or one of mycosis fungoides. Dr. Fox reported a case of a condition that

showed the clinical features of psoriasis for twenty-seven years but was finally proved to be mycosis fungoides. I am inclined to think that the case presented tonight is one of mycosis fungoides.

DR. HOWARD FOX: I think as Dr. Fraser does and agree with what the others have said. I believe that this is now mycosis fungoides which could be proved microscopically. Some years ago I reported the case of a man who had had psoriasis for twenty-eight years. He was under observation in my father's clinic and under Dr. Jackson's care. No one, however, thought that the man had anything but ordinary psoriasis. When I first saw him the lesions had changed in character and become elevated, suggesting mycosis fungoides. Dr. Pollitzer confirmed this diagnosis histologically. I do not know how it is possible to determine whether the present case has been one of a prefungoid type of mycosis fungoides all these years or a case of psoriasis undergoing mycotic changes. The differentiation would be merely a guess.

DR. WALTER J. HIGHMAN: Dr. Fox's concluding sentence is significant. I do not see how one can tell whether an eruption is prefungoid or not, except retrospectively when the diagnosis of mycosis fungoides has been established, whether the early outbreak was in the eczema group, the psoriasis group, the parapsoriasis group, the erythema group, as in Dr. Wise's case, the exfoliative dermatitis group or the prurigo group. What I think happens—and here I shall venture on a histogenic prophecy—is that the majority of chronic inflammatory diseases of the skin run their course with reference to the epidermis, the reticuloendothelial system always being somewhat involved. When, however, the reticuloendothelial system is particularly weak in its resistance, the habit of proliferation having developed, it ultimately leads to such a condition as mycosis fungoides. That is no established fact. It is not much more than a belief, but I think that along these lines will be found the explanation of the genesis of mycosis. Thus a great many of the inflammatory conditions which ab initio cannot be recognized as mycosis are in effect the forerunners of mycosis because of the peculiar let-up of resistant forces in the reticulo-endothelial system. This explanation harmonizes all the questions constantly arising in clinical conceptions of the disease and, more than that, explains the final development of the individual frankly mycotic lesion into sarcoma. Very frequently mycosis, as all the members know, ends with the appearance of sarcomatosis. Perhaps another link in this chain is conceivable as including Hodgkin's disease and leukemia. I heard the article referred to by Dr. Fraser, read by Dr. Hamilton Montgomery in Havana at the meeting of the American Dermatological Association. Many of Dr. Montgomery's remarks seemed to me to bear on my views.

DR. E. F. TRAUB: The reason I referred to the rather unusual case which I had the opportunity to follow was to emphasize the fact that all the lesions that suggested psoriasis disappeared with the onset of the tumor stage of the mycosis fungoides. I believe that this disappearance of the psoriatic lesions, incidentally without antipsoriatic treatment, with the fact that no such lesions reappeared up to the time of the patient's death—an interval of more than one year—is fairly good evidence that his trouble was mycosis fungoides right from the onset. I read the report of Dr. Fox's case carefully, and his was one of the few cases recorded in the literature in which some of the psoriatic lesions remained after the tumor stage of mycosis fungoides had set in. In such a case it would be difficult to rule out the possibility that mycosis fungoides was coincident with psoriasis.

DR. FRED WISE: This case was regarded as one of psoriasis for seven years by many local dermatologists. A second biopsy has not yet been made. I believe that there is a possibility of this being a case of psoriasis becoming "transformed" into mycosis fungoides. If it is, it is the third case of the kind which has been presented before the society. The first was the one presented by Dr. Fox. The second was that of a woman aged 45, under the care of Dr. MacKee and myself at the Vanderbilt Clinic, in whom the lesions of mycosis fungoides arose in the midst of previous patches of psoriasis. I remember especially one large patch on the knee, typically psoriatic for a number of years, which finally welled up into a tumor of mycosis fungoides, confirmed microscopically.

DR. GEORGE M. MACKEE: I should like to ask those who believe that psoriasis may eventuate in mycosis fungoides, thereby complicating the identity of each of the diseases, what becomes of the psoriasis? Why is there never any more psoriasis in the case of supposed authentic psoriasis when it becomes one of mycosis fungoides and the patient lives for a number of years? It is rare for psoriasis to disappear permanently. Therefore if the condition is really psoriasis, I should expect psoriatic lesions to be mingled with the mycotic lesions as long as the patient lives, but in all the cases on record there has been no psoriasis after the mycosis has developed. Therefore I question the transformation. I am rather inclined to think that in cases of mycosis preceded by lesions of the prefungoid stage resembling any one of the various inflammatory dermatoses the antecedent eruption is the early stage of mycosis fungoides and not a transformation from one disease to another. No one has yet learned how to make a histologic diagnosis in the very early stage.

DR. HOWARD FOX: May I ask why Dr. Abramowitz took that specimen for biopsy four years ago if he thought the eruption was ordinary psoriasis?

A CASE FOR DIAGNOSIS (ROSACEA-LIKE TUBERCULID OF LEWANDOWSKY?). Presented by DR. JOSEPH J. ELLER.

F. C., a male concert singer, presents markedly erythematous lesions on the nose, glabella and left cheek, of fifteen years' duration. The lesions are the size of a half dollar and are composed of coalesced papules and pustules with numerous telangiectases. There is a slight furfuraceous scaling with very slight evidence of atrophy and enlarged follicles over the glabella. Diascopic examination reveals complete blanching with no nodules or other pathologic features. The condition is subject to spontaneous exacerbation and remissions on which no effect has been exerted by sulphuric astringent lotions, roentgen rays and grenz rays. Intravenous administration of gold and sodium thiosulphate has produced slight but definite improvement in the past month. Examination of the blood and urinalysis show no alteration from the normal. The past history and the family history do not indicate tuberculosis. The patient is of athletic type, and no evidence of thoracic or other constitutional disease is discernible.

DISCUSSION

DR. FRED WISE: I agree with the diagnosis presented by Dr. Eller, on the basis of the history, the appearance of the lesions and the fact that the lesions respond to injections of gold preparations. A clinical differentiation between ordinary rosacea and the Lewandowsky tuberculid is very difficult unless one sees little nodules somewhat resembling the "apple jelly" nodules of lupus but more elevated. In this case there are a few nodules of that type. Taking into consideration the clinical appearance, the improvement under medication with gold preparations and the failure to improve under the orthodox treatment for rosacea, I believe that these points confirm the diagnosis. Serial tests with tuberculin would be corroborative.

DR. R. H. RULISON: This is an extremely interesting case. The isolated patch on the left cheek interests me. I think that there is a suggestion of atrophy there. Has that been noticed in a better light? I am inclined to agree with Dr. Eller's diagnosis of the case.

SCLERODERMA LICHENOIDES ("LICHEN ALBUS"). Presented by DR. FRED WISE.

F. D., a white married woman, aged 32, first came to the dermatologic clinic of the New York Post-Graduate Medical School and Hospital on Oct. 10, 1933, complaining of a localized hardening and discoloration of tissue on the back which had existed for the past eighteen months. At present there are on the upper part of the back, just to the left of the midline, two contiguous patches, each about the size of a silver dollar. The patches fade off into the surrounding skin, which

presents an erythematous halo. The lower patch is covered in part by a verrucous-like crusting, which is adherent. The surface of the patches is wrinkled and atrophied and exhibits fine yellow-brown plugs, characteristic of the disease. The thyroid gland is palpable.

The family history and the past history are irrelevant.

RECKLINGHAUSEN'S DISEASE. Presented by DR. PAUL E. BECHET.

H. F., a woman, aged 33, states that the lesions have been present for five years. In that interval they have increased enormously in number. The body is covered with innumerable verruca-like lesions and multiple fibromas. None of the lesions can be scraped off easily; on the contrary, it is almost impossible to scrape them off. Some of them are subcutaneous and others are distinctly fibrous, but they are all very small, and there are no apparent pigmented macules or plaques. The report of the pathologist confirms the tentative clinical diagnosis of Recklinghausen's disease.

DISCUSSION

DR. FRED WISE: I should not make a diagnosis of Recklinghausen's disease in this case. I should call the condition nevoid keratosis. I did not see soft tumors that could be pressed into the skin, leaving a baglike impression of the finger, or café au lait or blue spots. However, I did not make a sufficiently thorough examination to justify a definite diagnosis.

DR. JEROME KINGSBURY: I examined the patient rather carefully and did not find any evidence to warrant the diagnosis as presented.

DR. WALTER J. HIGHMAN: Whereas this probably does not fit into the picture von Recklinghausen described and hence is not Recklinghausen's disease, for the pigmentary reasons, as it were, that Dr. Wise mentioned, nevertheless the lesions which suggest keratoses do so only on a superficial glance. There are many unquestionable fibromas, soft, flat ones which can be moved on the surface over which they are attached to the skin. The scaly lesions do not give off their scales as in the seborrheic keratoses. I think that this is multiple fibromatosis, not Recklinghausen's disease, though it might be that, since the possibilities of variation cannot be exhausted. Under the microscope, with low power magnification, a curious edema of the connective tissue and of the papillae and subpapillary area is seen, which takes a bluish stain. Under the high power magnification, the edema is not unlike that observed in the early stages of the myxedematous change in fibroma.

DR. HOWARD FOX: I agree that this is not the picture of Recklinghausen's disease. The lesions suggest seborrheic keratoses, and appear as if they could be removed with a sharp curet, though Dr. Bechet says that they cannot. It is true that the patient is rather young for such changes. I think that the lesions represent some type of fibromatosis.

DR. J. FRANK FRASER: I examined the slide and could not find any evidence of either keratoses or neurofibromatosis. I did observe edema and rarefaction of the collagen fibers of the papillary and subpapillary layers. Whether this is an indication of a future neurofibromatosis is a question.

DR. PAUL E. BECHET: When I first saw this woman I thought that the lesions were seborrheic warts, but she is only 33 years old, and they have been present for five years. This sets the inception of the disease at the age of 28. It is most unusual to see hundreds of seborrheic warts in a person of that age. Dr. Wise is right: there are no spots of macular pigmentation. I tried to scrape off the little tumors, but did not succeed. On close examination some of these lesions resemble little fibrous tumors, and therefore I think that the condition is generalized fibromatosis. The most common type of generalized fibromatosis that I know is Recklinghausen's disease. Therefore, I made that diagnosis tentatively. The case was presented with that diagnosis partly on the pathologic report and partly on the clinical lesions.

DR. J. FRANK FRASER: Recklinghausen's disease is neurofibromatosis.

DR. WALTER J. HIGHMAN: I think that is substantially true, but it is difficult to establish that fact with the ordinary stains. This is a poorly selected specimen; it shows only changes below the epidermis.

"PERIPHLEBITIS NODULARIS NECROTICANS"(?); PAPULONECROTIC TUBERCULID (ABERRANT UNILATERAL ERUPTION ON THE LEG). Presented by DR. FRED WISE.

This man, aged 25, a native of Germany, first came to the dermatologic clinic of the New York Post-Graduate Medical School and Hospital on Oct. 10, 1933, stating that he had had an eruption on the lower part of the left leg for three years. The lower half of the left leg presents a number of round, crusted lesions situated on an erythematous base. The lesions are mainly on the posterior surface and are from ¼ to ½ inch (from 6 to 12 mm.) in diameter. Removal of the crust shows an ulcer, sharply defined, with a granulating base from which a slight purulent secretion exudes. The left shin shows a number of old scars. The patient states that during the past three years he has been free from lesions only for a period of about two months, which was about one year ago. He had one evanescent lesion on the right leg and one on the left lower quadrant of the abdomen. The individual lesions last about four months.

About four years ago the patient had a trivial injury to the left shin. A few years ago he suffered from severe night sweats. He denies having had a chronic cough or loss of weight, and states that there has not been any tuberculosis in the family, although his mother died of some sort of pulmonary inflammation.

Intradermal tests with old tuberculin in dilutions up to 1:1,000,000 were positive. A patch test with undiluted old tuberculin was 4 plus.

Biopsy showed deep tuberculosis associated with an intense edema of the walls of the blood vessels. Dr. Satenstein indicated that the term "perivasculitis associated with tuberculous granuloma" might well be applied to the histologic changes, rather than the name suggested by Török and others—"periphlebitis nodularis necroticans."

DISCUSSION

DR. J. FRANK FRASER: That is a very good tentative diagnosis, although a unilateral occurrence of this condition is rarely seen, and the condition is more common in the female sex. The diagnosis cannot be established without microscopic study.

DR. PAUL E. BECHET: I think I have presented to this society two cases with this diagnosis. The clinical picture was different. There were subcutaneous nodules in beadlike formation which were markedly indurated. The nodules were fixed to the overlying skin. As they underwent involution the skin was drawn down leaving a depression; the whole area was deeply pigmented, but the lesions never necrotized and broke down, as those in Dr. Wise's patient apparently have.

DR. HENRY H. WHITEHOUSE: I think that Dr. Wise mentioned Bazin's disease. I do not believe that the condition has anything in common with that. It has no relation to, and shows no clinical evidence of being, erythema induratum. I think that the unilateral character, as Dr. Fraser says, is unusual for periphlebitis nodularis. I believe, however, that the diagnosis is correct.

DR. WALTER J. HIGHMAN: The advantage of including the disease under discussion in the conception of Bazin's disease has never been clear to me. I think, too, that before it is decided that this is periphlebitis nodularis necroticans, it would be wise to make exhaustive studies into the possible parasitic nature of conditions other than tuberculosis in this patient. He shows a curious moth-eaten, channeled lesion. If he had come from a part of the country where madura foot prevails I should think the condition was almost identical with that. I mean infection with the fungus.

DR. FRED WISE: In reply to Dr. Bechet's discussion, I believe that two varieties have been described, one in which the nodule does not break down and subsequently suppurate, the type which Dr. Bechet mentioned, which results in depressed scars, and the other, which is the type I showed here tonight, which does break down, a process similar to what takes place in Bazin's disease.

A CASE FOR DIAGNOSIS (ERYTHROPLASIA OF QUEYRAT?). Presented by DR. BINFORD THRONE.

M. S., a man, aged 29, Jewish, has had red, elevated, sharply marginated plaques on the glans penis for ten months. They have resisted all local treatment. Examinations of the blood revealed nothing. The result of an intradermal test with tricophytin in the dilution of 1:10 on Oct. 20, 1933, was plus-minus. The report of the biopsy was as follows: "The section shows a marked inflammatory reaction. There is a thickened mucous membrane with long rete pegs. The upper derm shows a zone of cellular infiltration and engorged blood vessels. The inflammatory reaction is intense and superficial. The cellular exudate consists of plasma cells, lymphocytes and occasional polymorphonuclear cells. Many round cells have wandered into the epidermis. The deeper blood vessels are engorged and show no inflammatory exudate. There is no evidence of malignant or precancerous changes. The reaction is distinctly inflammatory."

DISCUSSION

DR. JOSEPH J. ELLER: I believe this to be a case of erythroplasia of Queyrat, similar to the case recently seen at the New York Post-Graduate Medical School and Hospital.

DR. FRED WISE: I am not qualified to speak of the microscopic section, but clinically I think that this is a replica of the case recently presented from the Post-Graduate Medical School and Hospital. The lesions do not heal under ordinary local treatment; the separate moist lesions fuse to become larger plaques; these features and the chronicity of the disease are characteristic. Clinically the lesion is erythroplasia.

DR. R. H. RULISON: I believe this is the same condition that has been shown here once before. The diagnosis of erythroplasia should be accepted.

ACNE INDURATA OF AN UNUSUALLY SEVERE TYPE. Presented by DR. PAUL E. BECHET.

J. S., a man, aged 22, has had for a number of years an acne indurata of such severe type that his face, neck and chest and the upper part of his back are entirely covered with great deep scars, some of which are almost 3 mm. in diameter. He has been completely disfigured by the disease.

DISCUSSION

DR. BINFORD THRONE: Some one in Europe, I think it was Ramel, reported finding acid-fast bacilli in cases of this type. About four or five years ago at the New York Skin and Cancer Hospital complement-fixation tests for tuberculosis were made in the diagnosis of different types of diseases of the skin, and in practically every case of severe acne which left marked scarring the result was 4 plus. That does not mean that a causal relationship exists between the two conditions, but it seems to me that patients with acne of this type should be considered as potentially tuberculous, and that systematic treatment should be instituted to see whether it may have any effect in preventing the development of tuberculosis in later life.

DR. PAUL E. BECHET: Since Dr. Throne has raised this point I want to agree with him most heartily. There is no question of a doubt that a low resistance, either of tuberculous or of other origin, is an essential factor in the causation of acne of this extraordinarily severe indurated type.

DR. R. H. RULISON: In certain cases of acne indurata remarkable improvement has followed the use of ammoniated mercury. I suggest this as a possible method of treatment.

SCLERODERMA OF THE LEFT SIDE OF THE FACE AND SCALP (HEMIATROPHY). Presented by DR. FRED WISE.

This girl, aged 9 years, came to the dermatologic clinic of the New York Post-Graduate Medical School and Hospital on Sept. 9, 1933, complaining of lesions on the face and scalp of one and one-half years' duration. About two years ago she suffered a moderately severe blow on the head just to the left of the bregma. About six months after this, the lesion on the scalp was noticed. At present the patient exhibits a yellowish-brown band, starting at about ½ inch (1 cm.) to the left of the medial end of the left eyebrow and immediately above the hair line and extending backward into the scalp for 5¾ inches (14.5 cm.) (ending just anteriorly to the vertex). The band varies from ¼ to ½ inch (6 mm. to 1 cm.) in width. At the edge of the scalp the band flares out into an area totally devoid of hair, 1 inch (2.5 cm.) long by ½ inch (1.2 cm.) wide. The skin over the involved parts feels hard and infiltrated. Some atrophy is present. The hair over most of the streak is sparse. The skin of the left cheek in an area extending from the angle of the mandible forward for 2 inches (5 cm.) and embracing about 4 square inches (25 sq. cm.) presents a similar involvement. Epicritic sensibility, as far as discrimination between two points is concerned, is impaired over the involved areas. The thyroid gland is palpable and appears to be slightly enlarged.

At birth the child was delivered by normal vertex presentation and her development has been normal. There have been no illnesses or traumas apart from the injury mentioned. There is no history of goiter in the family.

LUPUS VULGARIS OF THE FLAT, ATROPHIC TYPE (UNDER DIETETIC REGIMEN). Presented by DR. FRED WISE.

E. B., a white woman, aged 35, first came to the clinic of the New York Post-Graduate Medical School and Hospital on June 1, 1933, stating that she had lesions on the forehead of eighteen months' duration. At present she exhibits on both sides of the forehead, near the hair line, numerous pinhead-sized, salmon-yellow macular lesions which have become confluent and fused into plaques. There is one isolated pea-sized lesion at the left nasolabial fold and a similar one on the left ear. The skin in the affected areas is moderately atrophic; it is wrinkled like tissue paper and has a yellowish-brown tint.

A patch test with undiluted old tuberculin was negative. The Mendel-Mantoux test with 0.1 cc. of old tuberculin in dilutions of from 1:5,000 to 1:1,000,000 was negative. A roentgenogram of the chest showed marked lymphoid nodulation at the hilus and at the root of the lung. The histologic examination of the skin confirmed the clinical diagnosis. The patient was placed under the Hermannsdorfer-Sauerbruch salt-free diet, and in the past three months the skin has shown striking improvement. Local treatment was intentionally omitted.

DISCUSSION

DR. BINFORD THRONE: The results have been remarkable.

DR. HOWARD FOX: The result is certainly excellent and reminds me of the cases seen at the Copenhagen Congress and in Dr. Blumenthal's wards in Berlin.

DR. FRED WISE: This woman has improved, without exaggeration, 95 per cent since the dietetic treatment was begun. No other treatment has been given. Histologic examination revealed typical lupus vulgaris.

REPORT ON A CASE OF LYMPHANGIOMA SHOWN AT THE MEETING IN APRIL, 1933. Presented by DR. E. F. TRAUB.

At the April meeting of this society, I presented a boy, 5 years of age, who had a nevus situated in the skin and deeper tissues about the left knee. The condition had been clinically diagnosed as lymphangioma. This diagnosis was not acceptable because there was no microscopic confirmation. One of the lesions was excised, and biopsy has furnished the necessary histologic picture to fit this diagnosis.

BRONX DERMATOLOGICAL SOCIETY

HENRY SILVER, M.D., *Secretary*

Regular Meeting, Oct. 26, 1933

SAMUEL FELDMAN, M.D., *President, in the Chair*

PELLAGRA. Presented by DR. VAN ALSTYNE CORNELL and DR. MAX BERKOVSKY.

The patient, a white man aged 53, a porter, homeless and an alcoholic addict, was admitted to the Metropolitan Hospital about one month ago. The hospital record shows that he has been admitted at irregular intervals since 1928 (July, 1928; March, July and November, 1929; May, June and September, 1932, and June, 1933). He had many complaints, involving the oral cavity, the gastro-intestinal tract, the skin and the nervous system. Various diagnoses were made, such as eczema, alcoholic neuritis and cerebrospinal syphilis.

The examination of the gastro-intestinal tract revealed severe and persistent diarrhea with occult blood in the stool. There was moderate stomatitis. The tongue was red, the papillae enlarged. The patient complained of marked burning of the tongue. On the backs of both hands there was a severe dermatitis extending for about an inch up on the backs of the wrists. The area was sharply demarcated, crusty and brownish red.

The deep reflexes were normal. The Romberg sign was present. There was definite and marked hyperesthesia for pain and temperature. The sense of touch was not involved. The patient did not appreciate a prick in the distal part of the legs, but instantly reacted to a touch with a whisp of cotton. The hyperesthesia was limited to the legs and feet, while the thighs, arms, trunk and head were free. This dissociation of sensation and distribution speaks for a spinal disturbance and not for a disturbance of the peripheral nerve. The deep sensation was not involved.

The Wassermann reactions of the blood and spinal fluid were negative. The urine, the blood chemistry and the blood count revealed nothing abnormal. The gastric analysis showed complete achlorhydria, and examination of the stool showed occult blood.

PSEUDOPELLAGRA (ALCOHOLIC). Presented by DR. VAN ALSTYNE CORNELL and DR. MAX BERKOVSKY.

The patient, a white man aged 57, an alcoholic addict, was admitted to the Metropolitan Hospital on Oct. 14, 1933. The routine laboratory examination showed a negative reaction of the blood to a Wassermann test, normal urine and normal blood chemistry. The blood pressure was 120 systolic and 80 diastolic. The gastro-intestinal tract revealed no abnormalities. The backs of both hands showed marked dermatitis extending from the distal phalanges to about 2 inches (about 5 cm.) above the wrists, sharply defined. It began in the form of a vesicular eruption and then became crusty with denudation. There were marked subjective symptoms from the outset, with severe burning. The neurologic examination revealed that all forms of sensation, both superficial and deep, were intact.

DISCUSSION

DR. V. A. CORNELL: I regret to state that the lesions in the case of true pellagra have almost cleared. The patient had the typical triad of symptoms of this disease, namely the dermatitis, diarrhea and neurologic findings. The patient whom we present as having pseudopellagra shows only the cutaneous lesions of pellagra with no other manifestations.

DR. C. MARTIN: I believe that alcoholic pellagra, if it continues long enough, will simulate true pellagra to such an extent that one cannot tell them apart. This picture develops in many alcoholic addicts who go on a debauch for any length of time and abstain from food. A far better term for this disease than "pseudopellagra" would be "avitaminosis."

DR. F. CROSS: Pellagra is rare in private practice. It is encountered far more frequently in city hospitals. With respect to alcoholic pellagra, Klauder and Winkelman reported a series of cases in which the outstanding features were the dermatitis on the backs of the hands and in the V of the neck, with subsequent pigmentation and atrophy. Accompanying this were dementia, diarrhea and a red, beefy condition of the tongue. There was also the facies that typifies the alcoholic addict. The prognosis was usually poor.

DR. D. BLOOM: The patient whose condition was labeled true pellagra gave a history of huge consumption of alcoholic beverages. I am of the opinion that both patients present pseudopellagra on an alcoholic basis. Thus far it is difficult to decide whether the condition is avitaminosis or whether it is produced by the toxin of bad alcohol.

DR. M. BERKOVSKY: I do not believe that clinically one can differentiate true pellagra from pseudopellagra by means of the cutaneous lesions alone. The patient presented as having true pellagra impressed me as showing the outstanding triad of symptoms, which I have never found so clearcut in those with pellagroid symptoms. Furthermore, I think that the ultimate differentiation is based on the neurologic findings, and the latest belief is that the lateral columns are involved. This point has been demonstrated in the neurologic findings in the case of true pellagra. The etiology is entirely a matter of speculation. Some believe that spoiled corn produces pellagra. And the question arises whether or not the pseudopellagra found in chronic alcoholic addicts could not have been produced indirectly, in a modified form, from the corn used in the manufacture of alcohol.

SPASTIC PARAPLEGIA RESULTING FROM HEMANGIOMA OF THE BACK EXTENDING TO THE SPINE IN A PERSON WITH SYPHILIS. Presented by DR. HENRY SILVER.

This woman, aged 27, Jewish, came to the Mount Sinai Clinic, presenting a generalized eruption which was diagnosed as secondary syphilis. The Wassermann reaction of the blood was strongly positive. She was given two courses of arsphenamine and bismuth. During the first year the reactions of the spinal fluid and blood became negative. Last year she received the same courses of treatment. The Wassermann reaction of the blood was negative on three occasions. Gradually stiffness and pain developed in the thighs, especially in the left thigh. The lower extremities became so weak that standing and walking were impossible.

Examination revealed a large hemangioma about 15 by 10 cm., situated at the level of about the fifth to the twelfth thoracic vertebra, extending somewhat toward the left. There were also some pigmented areas on the inner side of the left arm and forearm, on the right arm and in a large area in the left groin over Scarpa's triangle. There were a few pigmented spots over the rest of the body and a raised pigmented mole over the sacrum.

The neurologic examination showed: a spastic paraplegia; knee jerk and ankle jerk exaggerated; abdominal reflexes absent; a bilateral Babinski reflex; motor power more involved in the left lower extremity, and a sensory level for all forms of sensation below the eighth dorsal segment, sparing the sacral area.

Examination of the spinal fluid on several occasions showed it to be normal. The blood showed: white cells, 8,100; hemoglobin 90 per cent; Wassermann reaction negative. The urine was normal; no arsenic was found. The blood pressure was 132 systolic and 84 diastolic. A roentgenogram of the hip showed slight atrophy of the head of the left femur, but no abnormality of the hip joint itself.

In view of the definite history of syphilis the clinical picture was thought to be a myelopathic process due to syphilis. The possibility of a vascular tumor of the dorsal region was considered. The patient continued to receive antisyphilitic treatment at the clinic. She felt well for three months and then noticed a return of stiffness of both legs. Soon she was unable to walk. Neurologic examination showed a definite sensory level at the fourth dorsal segment; there were exaggerated reflexes. Manometric tests showed a complete block. An exploratory operation was carried out on June 3, exposing the area from the third to the seventh dorsal segment, and there came into view a vascular extradural tumor, which was removed almost in its entirety. The postoperative course was satisfactory. On two different occasions manometric tests revealed no block. The spasmodic contractures disappeared, and the sensory level cleared up. The histologic diagnosis of the tumor was epidural hemangio-endothelioma.

BOWEN'S DISEASE. Presented by DR. THEODORE ROSENTHAL.

This woman, middle-aged, born in Canada, the mother of five children living and well, was admitted to Sydenham Hospital on Aug. 22, 1933. The present trouble began about nine years ago, when she noticed near the anus a small lump, which grew slowly. This was excised about four years ago, but recurred in the same location soon after the operation. On admission, the reactions of the blood to the Wassermann and Kahn tests were 2 plus. The patient received one course of antisyphilitic treatment. On Oct. 11, 1933, the reactions of the blood to the Wassermann and Kahn tests were negative. However, the lesions remained unchanged.

On the inner side of the right buttock, about 2 cm. from the anal margin, is a solitary red, moist, elevated, plaquelike lesion about 1.5 cm. in diameter, firm to the touch. The surrounding skin is unchanged. Sections from the lesion showed acanthosis, hyperkeratosis, clumping of nuclei in the epidermis and dyskeratosis. The histologic findings were characteristic of Bowen's disease.

DISCUSSION

DR. E. F. KELLEY: I examined the histologic slides. The outstanding feature was a dipping down of the epithelium and a lack of the palisade arrangement of the basal cell layer. Mitotic figures were abundant. The dyskeratosis was marked. In view of these findings the diagnosis of Bowen's disease should be accepted.

DR. C. WOLF: Although the histologic findings indicate Bowen's disease, it is extremely difficult to make the diagnosis clinically. The lesion is soft and mushy and suggests tuberculosis.

DR. S. FELDMAN: Clinically I should never venture that diagnosis. The slide shows some characteristics of Bowen's disease, but the acanthosis is of a more solid type, as seen in basal cell epithelioma.

DR. T. ROSENTHAL: The history of nine years' duration, the clinical appearance and the specific histologic appearances prove the diagnosis.

A CASE FOR DIAGNOSIS (GRANULOMA ANNULARE?). Presented by DR. GEORGE J. SPINNER.

This woman, married, aged 42, has three children living and well. There is a history of surgical interventions: (1) cyst of the ovary; (2) repair of a double hernia; (3) cholecystectomy and appendectomy. About ten months ago the patient noted several circular lesions on both arms. They began gradually to spread, so that at present they cover both arms, both legs and the trunk.

The entire picture is bizarre. Most of the lesions are concentric and vary in size from that of a dime to that of a quarter. Some lesions form circles; others form broken circles, or are semicircular or serpiginous. There are a number of rings within rings. All are sharply marginated. The border is thin and imperceptibly made up of small shiny papules. The center in some lesions is usually clear; in others, dull or pigmented. There are no subjective symptoms.

The laboratory examination, including a Wassermann test of the blood, disclosed no abnormality. The histologic examination revealed banal inflammatory changes.

DISCUSSION

DR. G. SPINNER: Following removal of a specimen for biopsy some of the lesions at the site faded. This speaks rather for granuloma annulare. One must also consider lichen planus annularis and erythema annulare centrifugum.

DR. S. PECK: I believe that it is lichen planus, for the lesions at the border are polygonal and bluish. I should like to see a section from the border. Erythema annulare Darier and granuloma annulare could be ruled out.

DR. I. M. LASHINSKY: I do not think that it is lichen planus annularis, as the rings are broken. I should say that it is granuloma annulare.

DR. F. CROSS. I suggest a diagnosis of a drug eruption resembling lichen planus. The patient gives a history of ingestion of phenolphthalein.

DR. L. CHARGIN: In analyzing this case, a great number of annular lesions, rings within rings and segments were observed. The border is slightly raised and appears to be papular. The center is somewhat scaly. Because of the scaling one must assume that the eruption is undergoing involution. I believe that it belongs to the group of multiform erythema, not of the Hebra type. I do not know of any drug that produces such an eruption.

DR. H. KEIL (by invitation): This may be a case of the disorder described by Jadassohn, namely, erythema circinatum, a condition which is allied to the urticarial group. I have seen a similar type of eruption in rheumatic fever.

DR. S. PECK: The final analysis will rest with the histologic picture. There is only one type of eruption resembling lichen planus that is produced by drugs, and that is the one caused by arsenic, and there is no history of ingestion of arsenic in this case.

DR. G. SPINNER: The patient has taken phenolphthalein, but a long time ago. In spite of that the eruption has been progressing, indicating that at least phenolphthalein is not responsible.

PEMPHIGUS VULGARIS TREATED WITH METHYLTHIONINE CHLORIDE (MACHT). Presented by DR. HENRY SILVER.

This man, aged 45, married, an operator of machines for making dresses, was admitted to the Bronx Hospital on Aug. 27, 1933. The patient has suffered from asthma for the past nine years and has submitted to an operation on the nasal septum. About a year ago the present eruption began with the appearance of a bullous lesion on the chest and back. About three weeks prior to admission the patient's condition became acutely aggravated. A large number of lesions appeared covering practically two thirds of his body. He was treated first with arsenic and then with large doses of viosterol.

At the time of admission the patient presented a foul-smelling, bullous and crusty eruption involving practically the entire body. The Nikolsky sign was positive. The face was swollen. The trunk showed alternating denuded and crusty areas. The oral cavity was markedly involved. The Pels-Macht phytotoxic test gave an index of 54 per cent. New bullous lesions appeared daily.

Repeated examinations of the urine gave negative results. The Wassermann reaction of the blood was negative. Blood counts showed 16,800 white cells and 4,460,000 red cells per cubic millimeter. The differential count showed polymorpho-

nuclears, 59 per cent; eosinophils, 3 per cent; band forms, 30 per cent; lymphocytes, 5 per cent; hemoglobin, 90 per cent. The blood chemistry revealed: dextrose, 108.1 mg.; uric acid, 3.7 mg., and urea nitrogen 16 mg. per hundred cubic centimeters. At the time of admission the patient's weight was 186 pounds (84.3 Kg.); temperature, 101.2 F.; pulse rate, 106, and respiration rate, 20. The blood pressure was 115 systolic and 60 diastolic.

On September 13, all previous therapy was discontinued and intravenous therapy with methylthionine chloride (methylene blue) was instituted. Cautiously, one-half ampule (5 cc.) was injected intravenously. Aside from a slight elevation of temperature to 102 F. there were no other reactions. Two days later the full dose of 10 cc. of a 0.5 per cent solution of methylthionine chloride was injected, and injections were continued every other day. The patient has received eighteen injections. The urine showed a blue color for thirty-six hours after the injections. Frequent examinations of the urine revealed nothing abnormal. The skin showed no abnormal discolorations. The sclerae and mucous membranes were normal. After the fourth injection of the dye new bullous lesions ceased to appear. The raw denuded areas began to heal rapidly and the patient's general condition improved greatly. During the past two weeks a severe itching has developed, which could hardly be controlled in spite of the administration of sedatives. The continuous scratching has somewhat retarded the rapid healing. After the fifteenth injection a specimen of blood was sent to Macht. The report showed a normal reading of 75 per cent. Two other specimens, taken a few days later, showed a reading of 74 per cent.

DISCUSSION

DR. L. CHARGIN: Following the brilliant results obtained by Ludy and his collaborators several patients at Mount Sinai Clinic were subjected to large doses of viosterol. The patients received as much as 44 cc. of viosterol a day for weeks without evident improvement.

It is well known that pemphigus runs a varied course. Remissions and even apparent cures occur with or without a variety of treatment. Thus, because of the uncertain course that this disease takes, one must be cautious in evaluating the efficacy of any form of therapy. I believe that it is too early to pass final judgment on therapy with methylthionine chloride.

DR. M. UMANSKY: Did other cases in which there was no treatment with methylthionine chloride show a better reading of the phytotoxic test during a remission? If during a spontaneous remission there is no change in the phytotoxic test, one may assume that this form of therapy is of value.

DR. F. CROSS: I have observed in cases of pemphigus improvement following high temperature, and suggest that the remission might be due to the reaction to the nonspecific protein. It is a question whether the improvement obtained in this case is due directly to the dye rather than to the reaction to the foreign protein.

DR. A. ROSTENBERG: Dr. Silver and I have under observation two patients with pemphigus who are treated with methylthionine chloride. In one case viosterol in large doses was tried without obtaining improvement. Methylthionine chloride was then resorted to, and it produced an excellent result. This form of therapy should have further trial.

DR. S. FELDMAN: I, too, had the opportunity to observe these patients. The patient presented by Dr. Silver came to the hospital in an aggravated condition. His condition improved visibly from day to day under treatment with methylthionine chloride. The second patient, whose condition is more chronic than that of the former, also showed remarkable improvement. We are continuing this form of therapy in other cases. The results are highly encouraging.

DR. H. SILVER: The improvement following treatment with methylthionine chloride was amply stressed by those who had the opportunity to observe the

patients. However, bearing in mind the course that pemphigus occasionally takes one must be cautious in evaluating particularly good results obtained with any new form of therapy.

NOTE.—Eight weeks following presentation the patient suffered a moderately severe relapse.

ICHTHYOSIS HYSTRIX WITH RADIUM SEQUELAE. Presented by DR. CHARLES A. GREENHOUSE.

This school girl, 11 years old, has had the present eruption since the age of 1 year. There was no history of cutaneous conditions of other members of the family. On both sides of the neck is a bandlike area of depigmented sclerotic skin, with mottled brownish pigmentation. There are similar changes under the right axilla, on the forearm and on the wrist. There is marked telangiectasia. On the right side of the trunk are linear verrucous brownish lesions in the direction of the lines of cleavage. There is a larger verrucous hyperkeratotic lesion on the right thigh, with bandlike areas of depigmentation, hyperpigmentation, telangiectasia and sclerosis. The child received twenty applications of radium seven years ago.

DISCUSSION

DR. C. WOLF: I diagnose nevus unius lateris.

DR. D. BLOOM: I am also of the opinion that the patient presents a verrucous nevus.

DR. V. A. CORNELL: The important point in cases of this type is not to use radium therapy. This patient presents the sequelae of a severe radium dermatitis.

DR. C. LERNER: I think that it is a nevus. Roentgen rays or radium should not be used in cases of this type, because nevi are very resistant to that form of therapy. Fulguration is better. The best results are obtained with excision and subsequent plastic repair, in order to avoid the formation of a basal cell epithelioma.

DR. C. GREENHOUSE: Of course it is a nevus. In labeling it ichthyosis hystrix, which is a nevus, the clinical character of the lesion is emphasized.

URTICARIA PIGMENTOSA AQUISITA IN A FULL-BLOODED INDIAN. Presented by DR. ADOLPH ROSTENBERG.

The patient was presented at the meeting of the section of dermatology of the New York Academy of Medicine in October, 1933.

DISCUSSION

DR. M. UMANSKY: The lesions in this case were irregular and about the size of a half-dollar. As a rule, urticaria pigmentosa presents lesions much smaller. Therefore I question the diagnosis and suggest a diagnosis either of a phenolphthalein eruption or of nevus pigmentosus.

DR. T. ROSENTHAL: I agree with the diagnosis as presented. The histologic section shows a large number of mast cells. This is characteristic of urticaria pigmentosa. It is true that mast cells may be found in other conditions, as nevi and Recklinghausen's disease, but not in such large numbers.

DR. J. A. LANAHAN (by invitation): I do not agree with Dr. Rostenberg that this patient is an Indian—West Indian would be more accurate. In other words, the patient is a Negro, and the lesions therefore should be judged with that fact in mind.

DR. A. ROSTENBERG: The lesions began as an urticaria with severe itching. Nevi do not start in a patient at this time of life and in this fashion. The shape does not deny urticaria pigmentosa, and the presence of mast cells further justifies my diagnosis.

MYCOSIS FUNGOIDES (PREMYCOTIC STAGE). Presented by DR. ADOLPH ROSTENBERG.

The patient, 72 years old, presents an eruption involving his right arm. It began four months ago. The area was scaling and itched severely. Soon the rash spread in an irregular way over different parts of the body. At no time have drugs been used, externally or internally.

On examination a widespread erythroderma was found in large, irregular patches, some of them markedly scaling and decidedly infiltrated. The patient complains of pain and severe itching.

Examination of the blood showed: hemoglobin, 103 per cent; erythrocytes, 5,120,000; leukocytes, 9,800; band forms, 8; segmented forms, 58; eosinophils, 2; lymphocytes, 24; monocytes, 8.

Biopsy showed marked hypertrophy of the epidermis, which sends irregular projections into the underlying connective tissue, in which are numerous scattered foci grouped around the blood vessels and also more diffusely. There is a variety of cells, consisting of mononuclear and endothelial cells, plasma cells, monocytes and lymphocytes. There are several areas of fibroblasts.

Apparently this is a granulomatous tissue with a tendency to perivascular infiltration. The absence of eosinophils speaks against mycosis fungoides. Pleomorphism speaks definitely against lymphatic infiltration.

DISCUSSION

DR. C. GREENHOUSE: I have studied the slides carefully and I tentatively diagnose mycosis fungoides.

DR. M. UMANSKY: I should like to mention a case of premycosis presented by Arzt of Vienna. The case was carefully studied histologically and no changes suggestive of mycosis fungoides were found. Later typical mycosis fungoides developed.

DR. C. WOLF: Highman maintains that one does not know where mycosis fungoides begins and where it ends. I challenge the statement that there is no such thing as premycosis.

DR. F. DIASIO: I think that the process is in the cutis, and if it is mycosis fungoides, it was there in the beginning.

DR. S. PECK: This case presents no histologic evidence warranting the diagnosis of mycosis fungoides. There are three important points to be considered: (1) the pale cell which must be present and which is usually detected in serial studies; (2) degenerative changes; (3) polymorphism. None of these is present here.

DR. L. CHARGIN: I have been interested for years in the relationship of mycosis and premycosis. It is my impression that there is a clinical stage which can be designated as premycosis and which is not characteristic histologically. Such cases terminate in true mycosis with typical histologic findings. Dr. Umansky's citation of Arzt's case points to a typical example.

DR. A. ROSTENBERG: I think that the slides are fairly characteristic, so that one can assume that the case is one of mycosis fungoides.

Directory of Dermatologic Societies *

FOREIGN

British Association of Dermatology and Syphilology (Canadian Branch)

Alberic Marin, President, Drummond Medical Bldg., Montreal.
Antonio Sabetta, Secretary-Treasurer, 3435 St. Denis St., Montreal.
Place: Hamilton, Ontario. Time: 1934.

Royal Society of Medicine, Section of Dermatology

Henry MacCormac, President, 23, Wimpole St., W. 1, London.
W. N. Goldsmith, Secretary, 6, Upper Wimpole St., W. 1, London.

NATIONAL DERMATOLOGIC SOCIETIES

American Medical Association, Scientific Assembly, Section on Dermatology and Syphilology

C. Guy Lane, Chairman, 416 Marlboro St., Boston.
Harry R. Foerster, Secretary, 208 E. Wisconsin Ave., Milwaukee.
Place: Cleveland. Time: June 11-15, 1934.

American Dermatological Association

Harold N. Cole, President, 1422 Euclid Ave., Cleveland.
W. H. Guy, Secretary, 500 Penn Ave., Pittsburgh.
Place: New York. Time: June 7-9, 1934.

SECTIONAL DERMATOLOGIC SOCIETIES

Baltimore-Washington Dermatological Society

Harry F. Anderson, President, 1610, 20th St. N.W., Washington, D. C.
Joseph V. Kennedy, Secretary, 1835 Eye St., Washington, D. C.

Central States Dermatological Association

Joseph Brumberg, President, 528 Delaware Ave., Buffalo.
William F. Hoover, Secretary, 333 Linwood Ave., Buffalo.
Place: Buffalo. Time: 1934.

Iowa and Western Illinois Dermatological Association

J. C. Kessler, President, University Hospital, Iowa City.
Robert E. Jameson, Secretary, 1014 First National Bank Bldg., Davenport, Iowa.

New England Dermatological Society

Rudolph Jacoby, President, 270 Commonwealth Ave., Boston.
J. Harper Blaisdell, Secretary, 5 Bay State Road, Boston.
Place: Boston. Time: April 11, 1934.

Southern Medical Association, Section on Dermatology and Syphilology

Thomas W. Murrell, Chairman, 17 E. Grace St., Richmond, Va.
C. C. Dennie, Secretary, Professional Bldg., Kansas City, Mo.
Place: San Antonio, Texas. Time: November, 1934.

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* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

STATE DERMATOLOGIC SOCIETIES

Florida Society of Dermatology and Syphilology

Chairman for each meeting is elected from city in which meeting is held.
Elmo D. French, Secretary, 602 Huntington Bldg., Miami.
Place: Jacksonville. Time: July 2, 1934.

Louisiana Dermatological Society

J. A. Devron, President, 150 Baronne St., New Orleans.
M. T. Van Studdiford, Secretary-Treasurer, 912 Pere Marquette Bldg., New Orleans.

Medical Society of the State of New York, Section on Dermatology and Syphilology

George M. Fisher, Chairman, 264 Genesee St., Utica.
Frank Combes, Secretary, 80 W. 40th St., New York.

Medical Society of the State of Pennsylvania, Section on Dermatology

Herbert J. Smith, President, 3303 N. 17th St., Philadelphia.
Robert L. Gilman, Secretary, 1930 Chestnut St., Philadelphia.

Michigan State Medical Society, Section on Dermatology and Syphilology

Robert C. Jamieson, Chairman, 1551 Woodward Ave., Detroit.
A. R. Woodburne, Secretary, Grand Rapids Clinic, Grand Rapids.
Place: Battle Creek. Time: September, 1934.

Minnesota Dermatological Society

D. D. Turnacliff, President, 407 Medical Arts Bldg., Minneapolis.
L. H. Winer, Secretary, 522 Medical Arts Bldg., Minneapolis.
Time: First Wednesday in October, December, February and April.

Oklahoma Dermatological Association

W. A. Showman, President, 108 W. 6th St., Tulsa.
C. L. Brundage, Secretary, 505 Osler Bldg., Oklahoma City.

Texas Dermatological Society

Everett C. Fox, President, 1719 Pacific Ave., Dallas.
Everett R. Seale, Secretary, 1215 Walker Ave., Houston.

LOCAL DERMATOLOGIC SOCIETIES

Atlanta Dermatological Society

Francis G. Jones, President, 384 Peachtree St., Atlanta, Ga.
Charles A. Wilkins, Secretary, Medical Arts Bldg., Atlanta, Ga.

Bronx Dermatological Society

Samuel Feldman, Chairman, 1955 Grand Concourse, New York.
Henry Silver, Secretary, 290 West End Ave., New York.

Brooklyn Dermatological Society

Arthur Persky, President, 1750 Ocean Parkway, Brooklyn.
George F. Price, Secretary, 884 Lincoln Place, Brooklyn.
Time: Third Monday of each month except June, July, August and September.

Buffalo-Rochester Dermatological Society

Earl D. Osborne, President, 471 Delaware Ave., Buffalo.
Richard L. Saunders, Secretary, 333 Linwood Ave., Buffalo.

Chicago Dermatological Society

James H. Mitchell, President, 25 E. Washington St., Chicago.
Max S. Wien, Secretary, 104 S. Michigan Ave., Chicago.

Cincinnati Dermatological Society

Harry L. Claassen, President, Provident Bank Bldg., Cincinnati.
Raymond G. Senour, Secretary-Treasurer, 19 W. 7th St., Cincinnati.

Cleveland Dermatological Society

S. Littman, President, 10515 Carnegie Ave., Cleveland.
H. G. Miskjian, Secretary, 856 Rose Bldg., Cleveland.

Detroit Dermatological Society

H. L. Keim, President, 10 Witherell St., Detroit.
William G. Saunders, Secretary-Treasurer, 9203 Grand River Ave., Detroit.

Los Angeles Dermatological Society

Stanley O. Chambers, Chairman, 727 W. 7th St., Los Angeles.
Nelson P. Anderson, Secretary, 2007 Wilshire Blvd., Los Angeles.

Manhattan Dermatologic Society

Howard Fox, Chairman, 140 E. 54th St., New York.
Mihran B. Parounagian, Secretary, 126 E. 39th St., New York.

Montreal Dermatological Society

J. F. Burgess, President, Drummond Medical Bldg., Montreal, Canada.
B. Usher, Secretary-Treasurer, 1538 Sherbrooke St., W., Montreal, Canada.

New York Academy of Medicine, Section of Dermatology and Syphilis

Leo Spiegel, Chairman, 241 W. 100th St., New York.
Eugene F. Traub, Secretary, 140 E. 54th St., New York.

New York Dermatological Society

Edward R. Maloney, President, 853 7th Ave., New York.
R. H. Rulison, Secretary, 145 E. 54th St., New York.

Omaha Dermatological Society

Alfred Schalek, Chairman, 721 Medical Arts Bldg., Omaha.
Donald J. Wilson, Secretary, 1216 Medical Arts Bldg., Omaha.

Philadelphia Dermatological Society

Jacques P. Guequierre, Chairman, 1930 Chestnut St., Philadelphia.
Robert L. Gilman, Secretary, 1930 Chestnut St., Philadelphia.

Pittsburgh Dermatological Society

Frederick Amshel, Chairman, 3401 5th Ave., Pittsburgh.
Bernhard Goldmann, Secretary, Jenkin's Arcade, Pittsburgh.

St. Louis Dermatological Society

Richard S. Weiss, President, 3720 Washington Blvd., St. Louis.
M. F. Engman, Jr., Secretary-Treasurer, 3720 Washington Blvd., St. Louis.

San Francisco Dermatological Society

H. J. Templeton, President, 3115 Webster St., Oakland, Calif.
John M. Graves, Secretary, 909 Hyde St., San Francisco.

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